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Treatment of Anogenital Warts: Siriraj Hospital Experience

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ABSTRACT

Objectives: To demonstrate the characteristics, treatment modalities and outcomes in the women presenting with Anogenital Warts (AGW) at Female STI Clinic, Siriraj Hospital.

Materials and Methods: The outcomes of treatment in the patients presenting with AGW who had complete follow-up at Siriraj Female STI clinic in 2016 were reviewed. The patients with immunocompromised conditions such as systemic lupus erythematosus and human immunodeficiency virus infection were excluded from this study.

Results: Two hundred and four of 217 women with AGW were eligible for this study. The mean age was 24.6 ± 5.2 years. Most of them were married and had sexual monogamy. Education levels were similar. Most of the AGWs were located outside the vagina and with ≤ 5 lesions (range 1-20). The diameter of warts was between 1 and 5 cm. The treatment modalities were 85% trichloroacetic acid (TCA) 131 (64.3%), 5% imiquimod 57 (27.9%), cryotherapy 8 (3.9%) and surgery 8 (3.9%). The median periods of treatment were 4, 8, 5 and 1 weeks for 85% TCA, 5% Imiquimod, Cryotherapy and Surgery, respectively. Treatment modalities were changed in the groups of 85% TCA and 5% Imiquimod, for 16.0% and 1.8%, respectively. Recurrence at 3 months after being cured was highest in the groups of 85% TCA (13.0%).

Conclusion: Our results showed that 85% TCA, which is widely available, need four applications with 13% recurrence rate. Imiquimod took longer time for treatment but was associated with less recurrent. Cryotherapy and Surgery showed promising results but the data were limit.

Keywords: anogenital warts, treatment.

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การรักษาหูดหงอนไก่บริเวณอวัยวะเพศและทวารหนัก: ประสบการณ์ ณ โรงพยาบาลศิริราช

มานพชัย ธรรมคันโธ, เจนจิต ฉายะจินดา

บทคัดย่อ

วัตถุประสงค์: *เพื่อแสดงให้เห็นถึงลักษณะ, สิ่งที่เลือกใช้ในการรักษา และผลของการรักษาในสตรีที่มาขอรับการรักษาหูดหงอนไก่บริเวณอวัยวะเพศและทวารหนัก ณ คลินิกโรคติดต่อทางเพศสัมพันธ์สตรี โรงพยาบาลศิริราช*

วัสดุและวิธีการ: *การศึกษาย้อนหลังจากข้อมูลในเวชระเบียนถึงผลการรักษาหลังจากสิ่งที่เลือกใช้ในการรักษาแต่ละสิ่ง ในปี พ.ศ. 2559 ซึ่งเป็นปีที่ซึ่งกำหนดนัดตรวจติดตามครบตามกำหนดนัดหลังการรักษา ณ คลินิกโรคติดต่อทางเพศสัมพันธ์สตรี โรงพยาบาลศิริราช เกณฑ์การคัดออก คือ สตรีที่มีหูดหงอนไก่บริเวณอวัยวะเพศและทวารหนัก แต่มีภาวะภูมิต้านทานร่างกายต่ำผิดปกติ เช่น โรคลูปัส และภาวะติดเชื้อไวรัสเอชไอวี*

ผลการศึกษา: *จากสตรีที่มีหูดหงอนไก่บริเวณอวัยวะเพศทั้งสิ้น 217 ราย เข้าเกณฑ์การวิจัยทั้งสิ้น 204 ราย ค่าเฉลี่ยของอายุ คือ 26.6 ± 5.2 ปี ส่วนใหญ่มีสถานภาพสมรส และมีคู่นอนเพียงคนเดียว ระดับการศึกษาพบกระจายใกล้เคียงกันในระดับต่างๆ ลักษณะรอยโรคของหูดหงอนไก่บริเวณอวัยวะเพศและทวารหนัก (ค่าพิสัย 1-20) ส่วนใหญ่พบเฉพาะภายนอกช่องคลอด จำนวนน้อยกว่าหรือเท่ากับ 5 รอยโรค เส้นผ่าศูนย์กลางของรอยโรคหูดหงอนไก่อยู่ระหว่าง 1-5 เซนติเมตร สิ่งที่ใช้เลือกนำมารักษาหูดหงอนไก่ประกอบด้วย 85 เปอร์เซ็นต์ กรดไตรคลออะซีติก (จำนวนผู้ได้รับ = 131); 5 เปอร์เซ็นต์ อิมิควิโมด (จำนวนผู้ได้รับ = 57) การรักษาด้วยการจี้เย็น (จำนวนผู้ได้รับ = 8) และการผ่าตัดโดยจี้ไฟฟ้าหรือผ่าตัดออก (จำนวนผู้ได้รับ = 8) ระยะเวลาการหายของรอยโรคหลังการรักษาคือ 4 (2-10) สัปดาห์, 8 (4-16) สัปดาห์, 5 (3-7) สัปดาห์ และ 1 สัปดาห์ ตามลำดับ ความจำเป็นที่จะต้องเปลี่ยนวิธีการรักษาพบในกลุ่มที่ได้รับ 85 เปอร์เซ็นต์ กรดไตรคลออะซีติก และ 5 เปอร์เซ็นต์ อิมิควิโมด เป็นร้อยละ 16 และ 1.8 การเกิดรอยโรคซ้ำหลังรักษาหายแล้ว 3 เดือน พบมากที่สุดในกลุ่มที่ได้รับ 85 เปอร์เซ็นต์ กรดไตรคลออะซีติก เป็นร้อยละ 13*

สรุป: *ความสัมพันธ์ในการรักษาโรคหูดหงอนไก่บริเวณอวัยวะเพศและทวารหนัก ไม่พบความแตกต่างมากนักในระหว่างสิ่งที่เลือกใช้ในการรักษา ณ คลินิกโรคติดต่อทางเพศสัมพันธ์สตรี โรงพยาบาลศิริราช*

คำสำคัญ: *หูดหงอนไก่บริเวณอวัยวะเพศและทวารหนัก, วิธีการรักษา*

Introduction

One of the world's most common sexually transmitted infections (STIs) is anogenital warts (AGW). It is mainly caused by non-oncogenic human papilloma virus (HPV) types 6 and 11[1]. These viruses were found to be closely related to cervical cancer. AGW is the most prevalence STI among young reproductive aged[2, 3]. In Thailand, the incidence of AGW was 6.03-6.80 per 100,000[4]. However, these figures are likely to be underestimated due to psychological burden, self-image and sexual-related concern[5]. At the Siriraj Female STI Clinic, Department of Obstetrics & Gynaecology, Faculty of Medicine Siriraj Hospital, Mahidol University, AGW is the mostly diagnosed by either visual diagnosis or tissue biopsy[6]. AGW can occur in any parts of the anal and genital areas with or without symptoms[7]. Posterior fourchette and labia minora appear to be the most common part[8]. Visible warts can cause physical discomfort such as itching, irritation, pain, burning, inflammation and bleeding during sexual activity. Also, psychological impact in women is resulted from these AGW. Some women are worried about the transmission of the warts and its recurrence, while the others have concerns about its interruption to their sexual life and relation with their sex-partners[5]. Although these low-risk HPV viruses rarely develop malignant transformation, successful treatment provides women with a better quality of life and relationship.

There are various treatment for AGW[9] ranging from ablative techniques, surgical excision, podophyllotoxin or trichloroacetic acid (TCA) to innovative topical treatment applied by the patients such as 5% imiquimod. The traditional measures were aimed to physical destruction of the warts lesion. Severe adverse events such as burning sensation, inflammation, pain, erosion, and itching can be occurred. Other modalities such as cryotherapy, laser vaporization, electrocautery and excision are painful and expensive as well as increase risks due to the viral particles floating during the procedures. In addition, recurrence of AGW is very common[9]. 5% Imiquimod is an immunomodulator that helps to increase eradication of viruses and lesions. It is to some extent superior to the other approaches in that it does not destroy the cell tissue at the warts areas, instead it modifies immune responses and stimulates binding of several induction-specific nuclear complexes[10]. Moreover, the reduction in the disease was found in earlier week of treatment in women using the different doses of the 5% imiquimod cream[11]. Combination of use of 5% imiquimod cream followed by surgery is reported to provide lower recurrence rates than only surgical approach[12]. As data in Thai population are limited, this study aimed to demonstrate our experience in treating Thai female patients presenting with AGW at Siriraj Hospital.

Materials and Method

This study was approved by Siriraj Ethical Review Board, Faculty of Medicine Siriraj Hospital, Mahidol University (COA. SI375/2018). Chart-review was conducted for the patients with AGW. Information of all female patients with AGW who received treatment at the Siriraj Female STI Clinic in 2016, the year that the follow-up system was fully settled, was extracted. The patients were excluded if they had immunocompromised conditions such as human immunodeficiency virus (HIV) infection and systemic lupus erythematosus (SLE).

In 2016, the Siriraj Female STI Clinic followed the 2015 Centers for Disease Control and Prevention STI treatment guideline[13]. Size and area coverage of the lesion were the first triage of the treatment. If the lesions involved larger than 10 cm^2, surgical removal would be the first choice of treatment. Application of 85% TCA solution was the most common treatment in our clinic. The patients were then follow-up once a week. If the condition was not improved after 5 visits, combination of 85% TCA and 5% imiquimod would be started. This treatment could be used up to 16 weeks and the patients would be monthly followed-up. Cryotherapy has been started in our clinic in late 2016. The patients in this group were also followed once a weeks.

Statistical analysis was performed by STATA version 12.1. Descriptive data were presented as N(%), mean ± SD and median with range.

Results

Two hundred and four out of 217 women presenting with AGW at the clinic, 204 were eligible for our study. Nine cases of HIV-infected and 4 cases of SLE were excluded. There were 83.3% of first-time AGW. Their mean age was 24.6 ± 5.2 years. Most of them were married and had sexual monogamy. Educational levels were similarly distributed. Most AGW were outside the vagina. Most patients had ≤ 5 lesions (range 1-20). The diameter of warts were 1-5 cm. Perianal warts were found in 7 women (3.4%) but only two of them had anal intercourse. None of the participants had HPV vaccination (Table 1).

Table 1. Demographic data of women with anogenital warts (N = 204).

Category	Frequency (N = 204)	Percent
Age of women (years)		
≤ 19	21	10.3
20 - 24	96	47.1
25 - 29	61	29.9
≥ 30	26	12.7
Marital status		
Single	57	27.9
Married	129	63.2
Divorced/ separated/ widow	18	8.8
Number of lifetime partners		
1	142	69.6
2	40	19.6
3	11	5.4
≥ 4	11	5.4
Level of education		
Primary school	39	19.1
Secondary school	61	29.9
Vocational school	43	21.1
University	61	29.9
First-time diagnosis of AGW	170	83.3
Experience of anal intercourse	2	1.0
Location of warts at first visit		
External	147	72.1
External + intravaginal	25	12.3
External + perianal + intravaginal	18	8.8
Intravaginal	7	3.4
Perianal	7	3.4
Number of warts at first visit		
≤ 5	132	64.7
6 - 10	47	23.0
11 - 15	14	6.9
≥ 16	11	5.4
Diameter of warts (cm)		
≤ 0.5	111	54.4
0.6 - 1.0	67	32.8
1.1 - 1.5	7	3.4
1.6 - 2.0	2	1.0
≥ 2.1	7	3.4
Treatment modalities		
Trichloroacetic acid	131	64.3
5% Imiquimod	57	27.9
Cryotherapy	8	3.9
Surgery	8	3.9

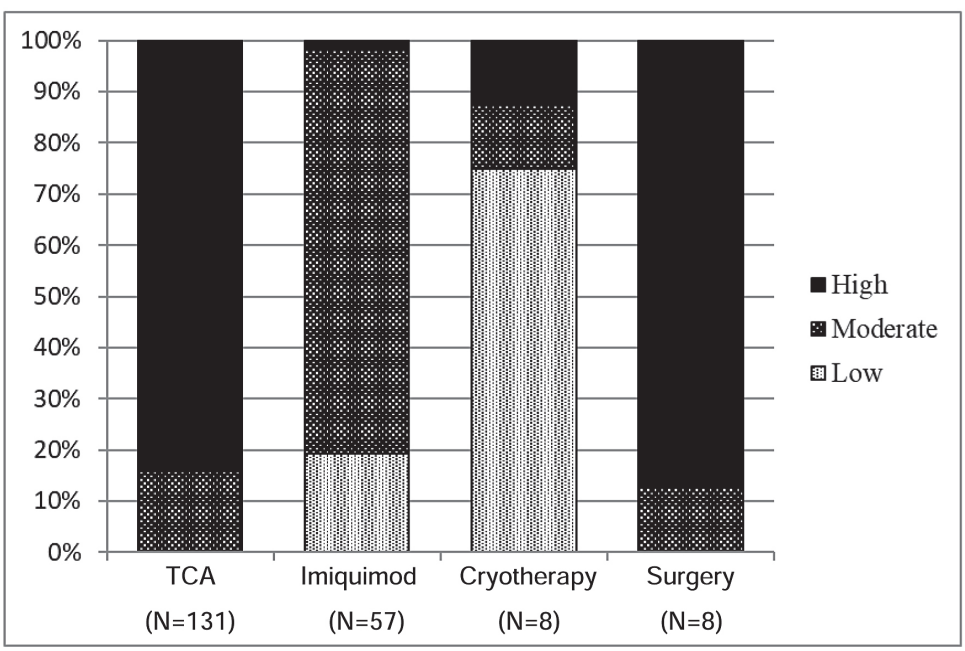
The treatment modalities included 85% TCA 131 (64.3%), 5% imiquimod 57 (27.9%), cryotherapy 8 (3.9%) and surgery 8 (3.9%). The median duration of treatment were 4, 8, 5 and 1 weeks for 85% TCA, 5% imiquimod, cryotherapy and surgery, respectively. Treatment were changed in the groups of 85% TCA and 5% imiquimod, at 16.0% and 1.8%, respectively. Recurrence rate after 3 months of successful treatment as highest in the 85% TCA group (13.0%) (Table 2). High degree of pain within 24 hours of treatment was most common in the patients receiving TCA and surgery (Fig. 1). Overall, patients had 'high' to 'very high' satisfaction for their treatment modality (Fig. 2).

Table 2. Treatment duration, change of treatment modalities and recurrence at 3 months after being cured (N = 204).

Treatment modalities	Treatment period (weeks)	Change of treatment modalities*	Recurrence at 3 months after being cured
Trichloracetic acid (N=131)	4 (2-10)	21/131 (16.0)	17/131 (13.0)
5% Imiquimod (N=57)	8 (4-16)	1/57 (1.8)	5/57 (8.8)
Cryotherapy (N=8)	5 (3-7)	0	0
Surgery** (N=8)	1	0	1/8 (12.5)

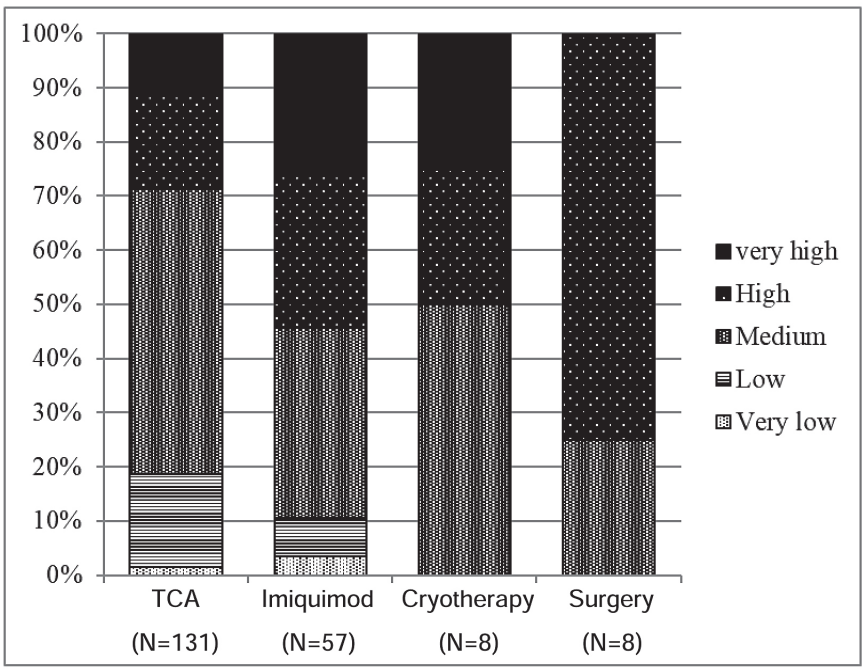
Data presented in N(%), median (minimum-maximum)

*Change of treatment modalities for 85% trichloracetic acid refers to adding 5% imiquimod to the weekly application of 85% trichloracetic acid.



TCA = 85% trichloracetic acid

Fig. 1. Degree of pain reported by the patients 24 hours following the application of treatment (N=204).



TCA = 85% trichloracetic acid

Fig. 2. Patients' satisfaction after using each treatment modality.

Discussion

Although the incidence of AGW at the Thai population is low[4], our finding suggests that the number may be underestimated. There were 170 new cases of AGW at our clinic in only one year. During the study period, our treatments were similar to the other health care units in Thailand by using 85 % TCA as the first choice. Imiquimod is currently available as an over-the-counter medicine. Contrasting to previous reviews[9], our results demonstrated high success rate of treatment in all measures. This may result from our service that include both treatment and health self-care counseling. Moreover, follow-up visits were also more frequent and regular.

These results were useful information to set up our guideline of treatments. TCA is the lowest cost, safe and widely available. Although most patients had high degree of pain within 24 hours, they were satisfied with the treatment. They concerned more about the treatment results than the side effects of medicine. The same findings were demonstrated in the surgical group.

The treatments of AGW are simple and applicable to medical students, residents and fellows. Our clinic has provided educational video on management techniques and counseling session. Some of this information can also freely accessible online. Cryotherapy provides impressive outcomes with less pain and shorter duration of treatment. This technique will be used more often for AGW in our clinic. Other novel treatments such as interferon, sinecatechins appear promising but they are not available in our clinic.

The incidence of AGW has been decreased in the countries that include quadrivalent (HPV 6, 11, 16, 18) or nonavalent (HPV 6, 11, 16, 18, 31, 33, 45, 52, 58) HPV vaccination as a national program such as Canada and Australia[14, 15]. This supports the results of the three landmark HPV studies, including FUTURE 1[16], Broad spectrum HPV[17] and V501-020[18]. The HPV vaccine against HPV type 6 and 11 do not only prevent new AGW cases but also alleviate the course of disease. Choi H compared Quadrivalent vaccine and surgical treatment in 26 Korean patients with AGW

and demonstrated that the recurrence rate was lower in the vaccine group[19]. Nonetheless, the present study can only represent information of unvaccinated population.

The well-planned follow-up schedule of patients with AGW in the specialized STI clinic, Siriraj Hospital is our the main strength. Our study is the first report on Thai female AGW patients. However, the treatment outcomes were depended on the experience and facilities of each center. Therefore, our low recurrence and high successful treatment may not represent the country data. In addition, the current study did not include HPV vaccinated population. Although AGW lesions have been cured following each treatment, the recurrence rate is still of concern.

Conclusion

Based on an experience of the Siriraj Female STI clinic, 85% TCA, which is widely available, needed for applications to treat AGW with 13% recurrence while 5% imiquimod took longer time for treatment with the side effects as immunomodulator i.e., redness, itching, swollen but was associated with lower recurrent rate. Cryotherapy and surgery appeared promising but the data were still limit.

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Potential conflicts of interest

The authors declare no conflict of interest.

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