Impact of Colposcopy-Guided Treatment of Recurrent Genital Warts on Patient's Quality of Life.



Medical Science

KEYWORDS: Recurrent Genital Warts; Colposcopy; Silver Nitrate Pencil; Quality of Life.

Anahita Nazempour	Gynecology Department, Behbood Hospital, Tabriz, Iran.
Neda asattarnejhad	Neuroscience Research Center (NSRC), Tabriz University, Tabriz, Iran.
Negar Yahyazade	Gynecology Department, Behbood Hospital, Tabriz, Iran.
Reza Mohammadian	Neuroscience Research Center (NSRC), Tabriz University, Tabriz, Iran.
Mohammad Asghari	Mohammad asghari, Department of Statistics and Epidemiology, Faculty of Health, Tabriz University of Medical Sciences, Tabriz, Iran
Laaya Firozan	Gynecology Department, Behbood Hospital, Tabriz, Iran.
Ali Tarighatnia	Msc student in Medical physics, Neurointervention Department, Aalinasab Hospital, Tabriz, Iran.
Hasan Shahrokhi	Clinical Psychiatry Research Center, Tabriz university of Medical sciences, Tabriz, Iran.

ABSTRACT

Introduction: Genital warts (GWs), due to association with increased cervical cancer risk and high recurrence rate, have deteriorating impacts on patient's quality of life (QOL). We investigated effects of colposcopy-guided cau-

terization of recurrent GWs on patient's QOL.

Methods& Materials: Women who were referred to our clinic with recurrent GWs were included. Colposcopic impression of cervix were evaluated and pap smear and colposcopic biopsy (if applicable) were taken. Apparent GWs were cauterized using a silver nitrate (SN) pencil under direct visual inspection. A standard QOLquestionnaire (WHOQOL-BREF) were filled by each individual before and 6-month after treatment. Results: Finally, 169 women with recurrent GWs and mean age of 35.78±8.82 years were included. Majority (90.5%) of cases hadn't previous history of GWs before last 6 months. Mean scores of QOL questionnaires in all assessed domains had improved considerably, after a 6-month follow up (P<0.001). No significant SN-related side effect was reported. No recurrence was detected during follow up period.

Conclusion Cauterization of recurrent GWs, using SN pencils, by direct visual inspection improved nations's OOL remarkably. Reducing

Conclusion: Cauterization of recurrent GWs, using SN pencils, by direct visual inspection improved patient's QOL, remarkably. Reducing treatment duration and number of visits, decreasing recurrence rate and cost of treatment can be the main factors of this finding.

Introduction:

Genital warts, also known as "condylomataacuminata", are one of the most prevalent sexually transmitted diseases (STD) (1,2). Although, not a life-threatening condition, their association with certain types of HPV infection and increased risk of cervical cancer, makes GWs a matter of concern (3, 4). Unknown course and uncertainty of treatment, high recurrence rate, correlation with malignancy, on the other hand, anxiety about disease transmission, effects on sexual life and social relationships, all, have negative impacts on patient's quality of life (QOL), which can adversely affect patient adherence (5-10). Commonly used medical treatment, such as Podophyllin, Imiquimod, etc., have long duration of treatment with variable success rate, also, local and systemic side effects, which necessitate development of more efficacious novel guidelines for elimination of GWs (11-14).Cauterization with silver nitrate (SN) pencils has been reported to be superior to commonly used medications for this purpose, with shorter treatment-duration, lower re-incidence and higher costefficacy(15); however, there is a lack of quantitative data on effects of this approach on patient's satisfaction and QOL. This study investigated impact of colposcopy-guided chemical cauterization of recurrent GWs by direct visual inspection, on patient's QOL.

Methods & Material:

This prospective interventional cohort study was conducted on women referred to gynecology clinic of Behbood Hospital (Tabriz, Iran) with recurrent genital warts. Despite undergoing, at least, one thorough course of treatment with grade A drugs (Podophyllotoxin 0.05%-15% solution, gel or cream, Imiquimod 3.75-5% cream, Sinecatechins 15% ointment) according to the Agency for Health Care Policy and Research guideline (AHCPR 1994) and 2012 European guideline for the management of anogenital warts(16), the patient had reappearance of warts in vulva,

perineum(the area between anus and vaginal orifice) and walls of vagina or cervix, in less than 6 months.

Before the patient's inclusion, the process and aims of study, also, the possible side effects of SN application (skin color change, burns,etc.) were explained by the gynecologist. After obtaining informed written consent, the individual was included. A demographic data check list (inquiring about current age, age at first sexual intercourse, method of contraception, history of warts before last 6 months) and the World Health Organization Quality of Life-BREF(WHOQOL-BREF)questionnaire,were filled out by the patient before commencement of the procedure.

Colposcopic evaluation was carried out for accurate visual inspection of cervix and walls of vagina (on 7th day of last menstrual period). Infiltration of lidocaine hydrochloride 2% (without epinephrine) was done for local anaesthesia, prior to colposcopy. The colposcopic impression was recorded and biopsy was taken from suspicious areas after application of 5% acetic acid solution (with/without endocervical curettage) for further study. Concomitant Pap smear specimen was obtained, for evaluating concordance of results of two tests (colposcopic biopsy vs Pap smear test). Apparent warts were directly cauterized using a SN pencil (silver nitrate BP 95% w/w, potassium nitrate BP 55% w/w). Hemostasis was performed by the same SN pencil or suturing, in the case of any bleeding.

All patients were revisited every 3 weeks for re-cauterization of apparent warts, if needed. Finally each case underwent a 6-month follow-up. The patient was recommended to call the gynecologist in the case of having any problem. The WHOQOL-BREF was refilled by the patient at 6th-month follow-up.

SPSS version 13 (SPSS Inc., IL, Chicago, USA) were used for data analysis. The results of qualitative analysis were reported as frequency and percent. Quantitative findings were published as mean± standard deviation (S.D) or 95% confidence interval, if applicable. Scores of each domain of QOL questionnaire, acquired before and 6 months after intervention, were compared using paired-sample t-test. P value <0.05 was considered statistically significant.

Results:

Finally, 169 women with recurrent GW and mean age of 35.78±8.82 years, were included. Average age of first sexual intercourse was 19.68±3.89.Data on methods of contraception, presence of postcoital bleeding, history of GW before last 6 months are summarized in Table 1. As an isolated item, male condom was the most commonly used contraceptive method (22.5%). Most investigated cases had not postcoital bleeding (81.7%) and 90.5% had not any history of GWs before last 6 months. Pap smear test results and the relevant colposcopic findings are exhibited in Table2 and 3: only 27.8% of cases had normal cervical impression and most prevailing finding was cervical ulcer (33.7 %). QOL-scores of cases before and 6 months after colposcopyguided cauterization of warts, were calculated in each of 4, physical health, psychological, social relationships and environment domains and compared (Table 4), which showed considerably improved scores in all domains (P<0.001). Cross-comparison of Pap smear test and colposcopic biopsy results are outlined in Table 5. No SN-related side effect was reported.

Discussion:

In this paper, we report impacts of colposcopy-guided treatment of recurrent GWs on QOL of the patient, after a 6-month follow up.

According to our findings, cauterization of recurrent GWs with SN pencils under direct visual inspection, improved patient's QOL-scores in all, physical health, psychological, social relationships and environment domains.

Anxiety about HPV-related increased cancer risk, disease transmission and its effects on social and sexual relations, causes feeling of anger, fear, guilt and depression in affected individuals (17-20). Having a highly contagious venereal disease with long treatment course, unknown therapeutic outcome and high incidence of recurrence, has the most significant adverse psychologic effects, which impoverishes patient's QOL (5, 6,22,23).

Self-administered topical therapies (Imiquimod, Podofilox) are the first drugs of choice for treatment of GWs; however, prolonged treatment, high possibility of recurrence, local and systemic side effects (pruritis, nausea, etc.) limit patient compliance and adherence(11, 23,24). Healthcare-provided surgical procedures (excision, electro surgery, etc.), although more effectual in management of GWs, are the second line of treatment due to cost, availability, pain and scarring, like other surgical operations(25-29).

Silver nitrate compounds have been efficacious in treatment of non-genital warts (30,31)

Lwegaba and colleagues, report SN cauterization of GWs (1-3 applications) to be superior to any other existing agent for this purpose. Clearance rate of warts with SN was 93% (vs. 17.7% of Podophyllin); the mean cost of healing with SN was 28.47 US \$ per patient (16.15 US \$ /visit), compared to 598 US \$by podophyllin(14.32 US \$ / visit) in India. More satisfaction, no recurrence and less irritation was reported by SN group (32), which was in concordance with outcomes of our study. SN was more successful, economic and easily applicable in treatment of warts than other topically administered drugs (31, 32).

Although, deteriorating effects of GWs on patient's QOL has been confirmed (33, 34), due to lack of related data, comparing effects of

SN treatment on patient's QOL with similar reports was impossible.

According to collected data, most frequently used methods of contraception were barriers (cervical cap, female condom, etc.), other than male condom (27.2%); however, as an isolated item, male condom was the most commonly used contraceptive method (22.5%). Based on available literature, condoms are the most effective appliance in reducing sexually transmitted infections, including HPV(35, 36). The possible cause of this discrepancy is inappropriate usage of condoms, due to poor education and low educational level. An alternative explanation is beginninguse of condoms after being infected with GWs (37).

Certain types of HPV infection are associated with increased risk of developing cervical cancer (38). Although Pap smear test has been efficient in finding premalignant and malignant lesions of squamous cell carcinoma, it has been less successful in detecting premalignant lesions in high risk population (39). Jernimo et al report correlation of HPV DNA, especially carcinogenic type 16, with visual abnormalities of cervix, regardless of histologic findings (39). In our study among patients with normal Pap smear test, only 20.7% had normal cervical appearance and 21.9% of whom underwent biopsy (due to abnormal colposcopic impression) had normal biopsy results.

Colposcopy-guided treatment of GWs, under direct visual inspection, made concomitant assessment of premalignant cervical lesions, possible, which could be missed by Pap smear test alone in this high-risk group. Acetic acid application, helps with locating highly suspicious areas for biopsy improving quality of colposcopic evaluation for detecting abnormaltissue (40).

To our knowledge, it is the first study investigating effects of chemical cauterization of recurrent GWs on patient's QOL, on quantitative basis.

The main limitation of our study was lack of control group treated with other topical or surgical procedures.

Further controlled trials, with larger sample size and longer follow-up periods, are mandated to confirm or refute findings of this study.

Conflict of interest: we declare that we have no conflicts of interest.

		Frequency	Percent (%)
Method of		0000000000	
Contraception			
	VS	-7	4.1
	TL.	13	7.7
	Barriers*	46	27.2
	Male Condom	38	22.5
	OCP	19	11.2
	IUD	9	5.1
	Menopause	11.	6.5
	Pregnant	1	0.6
	None	75	14.8
PCS			
	Yes	31	18.3
	No	138	81.7
History of GWs			
	Yes	16	9,5
	No	153	90.5

Table1: Demographic data regarding methods of contraception, postcoital bleeding (PCB), history of genital warts (GWs) before last 6 months. VS: Vasectomy. TL: Tubal Ligation. OCP: Oral Contraceptive Pills. IUD: Intrauterine Device.* "Barriers" mean barrier methods other than male condom, such as diaphragm, female condom, cervical cap, etc

		Biopsy									
		No Biopsy		Chronic Cervicitis	Acute Cervicitis	Metaplasia	Atypia	CIN1	CIN2	Total	
Pap Smear	Normal	35	37	15	11	3	3	17	1	122(72.2%)	
	Inflammation	5	7	3	1	0	0	6	0	22(13%)	
	ASCUS	3	1	4	1	0	0	4	0	13(7.7%)	
	CIN1	1	0	5	2	0	0	3	1	12(7.1%)	
	CIN2	-	-	-	-	-	-	-	-	-	
Total		44(26%)	45(26.6%)	27(16%)	15(8.9%)	3(1.8%)	3(1.8%)	30(17.7%)	2(1.2%)	169(100%)	

REFERENCE

1. Fleurence, Rachael L., Julia M. Dixon, Tsveta F. Milanova, and Kathleen M. Beusterien. "Review of the economic and quality-of-life burden of cervical human papillomavirus disease." American journal of obstetrics and gynecology 196, no. 3 (2007): 206-212. | | 2. Lacey, Charles JN, Catherine M. Lowndes, and Keerti V. Shah. "Burden and management of non-cancerous HPV-related conditions: HPV-6/11 disease." Vaccine 24 (2006): S35-S41. | | 3. Mortensen, Gitte L., and Helle K. Larsen. "The quality of life of patients with genital warts: a qualitative study." BMC Public Health 10, no. 1 (2010): 113. | | 4. Wright, Thomas C., F. Xavier Bosch, Eduardo L. Franco, Jack Cuzick, John T. Schiller, Geoffrey P. Garnett, and André Meheus. "HPV vaccines and screening in the prevention of cervical cancer; conclusions from a 2006 workshop of international experts." Vaccine 24 (2006): S251-S261. | | 5. Reitano, M. D. "Counseling patients with genital warts." The American journal of medicine 102, no. 5 (1997): 38-43. | | 6. Ireland, Juliet A., Murray Reid, Rachael Powell, and Keith J. Petrie. "The role of illness perceptions: psychological distress and treatment-seeking delay in patients with genital warts." International journal of STD & AIDS 16, no. 10 (2005): 667-670. | | 7. Hammarlund, Kina, Ingela Lundgren, and Maria Nyström. "To contract genital warts—A risk of losing love? Experiences of Swedish men living with genital warts." International Journal of Men's Health 6, no. 2 (2007): 100-114. | | 8. PERSSON GÖRAN, LARS GOSTA DAHLOF, and INGELA KRANTZ. "Physical and psychological effects of anogenital warts on female patients." Sexually transmitted diseases 20, no. 1 (1993): 10-13. | | 9. Voog, E., and G. B. Löwhagen. "Follow-up of men with genital papilloma virus infection. Psychosexual aspects." Actadermato-venereologica 72, no. 3 (1991): 185-186. | 10. Jeynes, C., M. C. Chung, and R. Challenor. "Shame on you'-the psychosocial impact of genital warts." International journal of STD & AIDS 20, no. 8 (2009): 557-560. | | 11. Bonnez, William. "Human Papillomavirus." http://www.antimicrobe.org/new/v15. asp | | 12. Bonnez W, Elswick RK Jr., Bailey-Farchione A, Hallahan D, Bell R, Isenberg R, Stoler MH, Reichman RC. Efficacy and safety of 0.5% podofilox solution in the treatment and suppression of anogenital warts. Am J Med 1994;96:420-425. | | 13. von Krogh G, Longstaff E. Podophyllin office therapy against condyloma should be abandoned. Sex Transm Infect 2001;77:409-12. | | 14. Hellberg D, Svarrer T, Nilsson S, Valentin J. Self-treatment of female external genital warts with 0.5% podophyllotoxin cream (Condyline) vs weekly applications of 20% podophyllin solution. Int J STD & AIDS 1995;6:257-261. | | 15. Shankar, Sonal, and Jane Sterling. "Nongenital warts: recommended approaches to management." Prescriber 18, no. 4 (2007): 33-44. | 16. Lacey, C. J. N., S. C. Woodhall, A. Wikstrom, and J. Ross. "2012 European guideline for the management of anogenital warts." Journal of the European Academy of Dermatology and Venereology 27, no. 3 (2013): e263-e270. | | 17. Smith, Jennifer S., Lisa Lindsay, Brooke Hoots, Jessica Keys, Silvia Franceschi, Rachel Winer, and Gary M. Clifford. "Human papillomavirus type distribution in invasive cervical cancer and high-grade cervical lesions: A meta-analysis update." International journal of cancer 121, no. 3 (2007): 621-632. | | 18. Maw, Raymond D., Michael Reitano, and Michel Roy. "An international survey of patients with genital warts: perceptions regarding treatment and impact on lifestyle." International journal of STD & AIDS 9, no. 10 (1998): 571-578. | | 19. Cox J. Thomas, Karl-Ulrich Petry, Eva Rylander, and Michel Roy. "Using imiquimod for genital warts in female patients." Journal of Women's Health 13, no. 3 (2004): 265-271. | 20. Badia Xavier, Jose A. Colombo, Nuria Lara, M. Angels Llorens, Luis Olmos, Miguel S. de los Terreros, Jose A. Varela, and Juan J. Vilata. "Combination of qualitative and quantitative methods for developing a new Health Related Quality of Life measure for patients with anogenital warts." Health and quality of life outcomes 3, no. 1 (2005): 24. | | | 21. Woodhall Sarah, Tina Ramsey, Chun Cai, Simon Crouch, Mark Jit, Yvonne Birks, W. John Edmunds, Rob Newton, and Charles JN Lacey. "Estimation of the impact of genital warts on health-related quality of life." Sexually transmitted infections 84, no. 3 (2008): 161-166. | | 22. Mortensen, Gitte Lee. "Long-term quality of life effects of genital warts: a follow-up study." Dan Med Bull 57, no. 4 (2010): A4140. | | | 23. Frega, A., P. Stentella, F. Renzi, L. DelleChiaie, L. Cipriano, and A. Pachi. "Assessing the control of th ment of self application of four topical agents on genital warts in women." Journal of the European Academy of Dermatology and Venereology 8, no. 2 (1997): 112-115. | 24. Fisher, A. A. "Severe systemic and local reactions to topical podophyllum resin." Cutis; cutaneous medicine for the practitioner 28, no. 3 (1981): 233-236. | | 25. Stone, K. M., T. M. Becker, A. Hadgu, and S. J. Kraus. "Treatment of external genital warts: a randomised clinical trial comparing podophyllin, cryotherapy, and electrodesiccation." Genitourinary medicine 66, no. 1 (1990): 16-19. | | 26. Khawaja, H. T. "Podophyllin versus scissor excision in the treatment of perianal condylomataacuminata: a prospective study." British journal of surgery 76, no. 10 (1989): 1067-1068. | 27. Sherrard Jackie, and Lynn Riddell. "Comparison of the effectiveness of commonly used clinic-based treatments for external genital warts." International journal of STD & AIDS 18, no. 6 (2007): 365-368. | | | 28. Handley J. M., R. D. Maw, T. Horner, H. Lawther, T. McNeill, and W. W. Dinsmore. "Non-specific immunity in patients with primary anogenital warts treated with interferon alpha plus cryotherapy or cryotherapy alone." Actadermato-venereologica 72, no. 1 (1991): 39-40. | | 29. Hussain Fawad, and Anthony Ormerod. "Nongenital warts: Recommended management in general practice." Prescriber 23, no. 6 (2012): 35-41. | | 30. Ebrahimi S., N. Dabiri, E. Jamshidnejad, and B. Sarkari. "Efficacy of 10% silver nitrate solution in the treatment of common warts: a placebo-controlled, randomized, clinical trial." International journal of dermatology 46, no. 2 (2007): 215-217. | | 31. Ba aran E, "Efficacy of silver nitrate pencils in the treatment of common warts." The Journal of dermatology 21, no. 5 (1994): 329-333, | 32, Lwegaba A, A, Phillips, and R, Kiraru, "Silver nitrate may be far superior to podophyllin in clearing HPV external anogenital warts." West Indian Medical Journal 57, no. 1 (2008): 63-65. | | 33. Marra Carlo, Gina Ogilvie, Louise Gastonguay, Lindsey Colley, Darlene Taylor, and FawziahMarra. "Patients with genital warts have a decreased quality of life." Sexually transmitted diseases 36, no. 4 (2009): 258-260. | 34. Drolet Mélanie, Marc Brisson, Elizabeth Maunsell, Eduardo L. Franco, François Coutlée, Alex Ferenczy, Sam Ratnam, William Fisher, and James A. Mansi. "The impact of anogenital warts on health-related quality of life: a 6-month prospective study." Sexually transmitted diseases 38, no. 10 (2011): 949-956. | | 35. Hogewoning, Cornelis JA, Maaike CG Bleeker, Adriaan JC van den Brule, Feja J. Voorhorst, Peter JF Snijders, Johannes Berkhof, Pieter J. Westenend, and Chris JLM Meijer. "Condom use promotes regression of cervical intraepithelial neoplasia and clearance of human papillomayirus; a randomized clinical trial," International Journal of Cancer 107, no. 5 (2003); 811-816. | 36, McIlhaney Ir. Joe S. "Sexually transmitted infection and teenage sexuality." American journal of obstetrics and gynecology 183, no. 2 (2000): 334-339. | | 37. Guerreiro, D., M. A. M. Gigante, and L. C. Teles. "Sexually transmitted diseases and reproductive tract infections among contraceptive users." International Journal of Gynecology & Obstetrics 63 (1998): S167-S173. | | 38. Dalstein, Veronique, Didier Riethmuller, Jean-Luc Prétet, Karine Le Bail Carval, Jean-Loup Sautière, Jean-Pierre Carbillet, Bernadette Kantelip, Jean-Patrick Schaal, and Christiane Mougin. "Persistence and load of high-risk HPV are predictors for development of high-grade cervical lesions: a longitudinal French cohort study." International journal of cancer 106, no. 3 (2003): 396-403. | 39. Jeronimo, Jose, L. Stewart Massad, and Mark Schiffman. "Visual appearance of the uterine cervix: correlation with human papillomavirus detection and type." American journal of obstetrics and gynecology 197, no. 1 (2007): 47-e1. | | | 40. Chase, Dana M., Marlene Kalouyan, and Philip J. DiSaia. "Colposcopy to evaluate abnormal cervical cytology in 2008." American journal of obstetrics and gynecology 200, no. 5 (2009): 472-480.