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Original Article

A Randomized Clinical Trial of Cryosurgery with Nobothian Cyst Drainage for the Recurrent Cervicitis Treatment

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ABSTRACT

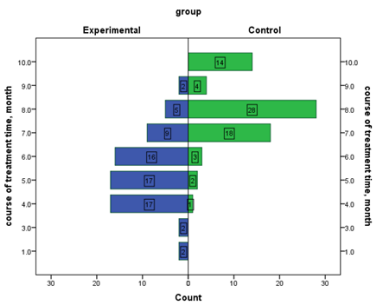
Objectives: To compare the effect of cervical Cryosurgery (cryotherapy) along with draining of nabothian cysts with sole Cryosurgery in chronic Cervicitis.

Methods: This was a randomized parallel clinical trial study conducted on 144 patients with nabothian cysts referred to a Gynecology (GYN) clinic in Jahrom city, south of Iran, due to chronic Cervicitis. The patients were randomly divided into case and control groups treated with cryotherapy and antibiotic therapy with and without drainage of nabothian cysts, respectively. The primary study outcomes were subjective symptoms and duration of the treatment to complete improvement that was followed every month till three months. Data were analyzed using SPSS.

Results: One-hundred forty patients were recruited in Experimental (n=70) and control (n=70) groups who were matched for Sociodemographic characteristics (P>0.05). McNamara's test showed a statistically lower occurrence of all subjective symptoms in the pre-and post-intervention in both experimental and control groups (P<0.001). The mean duration of the treatment course in the experimental group was 5.4±1.59 months, while it was 7.91±1.59 months in the control group. There was a significant difference between the two groups in the duration of treatment (P<0.001). In the linear regression of the study variables, none of the variables expect the groups significantly predicted the duration of treatment, t=9.87, P=0.001.

Conclusion: We found the new method of nabothian cysts drainage along with cryotherapy effective and the cryotherapy alone; it showed a shorter duration of the treatment to achieve complete improvement. Therefore, considering this method, the required frequency of Cryosurgery might decrease.

GRAPHICAL ABSTRACT



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Introduction

Cervicitis is common in young sexually active women and corresponds to the inflammation of the uterine cervix that primarily impacts the endocervical glands' columnar epithelial cells [1]. Moreover, Cervicitis is divided into acute and chronic Cervicitis depending on whether it is caused by an infectious or non-infectious origin [2]. Acute Cervicitis is usually a result of an infection (Chlamydia, gonorrhea). In contrast, chronic Cervicitis appears to have a non-infectious source and is defined as the cervix's chronic or persistent inflammation [1,2]. Nabothian cysts are frequent and quiet retaining cysts of the uterine cervix that do not require medical attention in most cases and are found in chronic cervicitis patients [3,4]. Nabothian cysts are benign, full-bodied, and precise cysts in cervix. There may be more than one Nabothian cyst in a person's body. These cysts may occur in women after childbirth or during menopause. The presence of these cysts does not necessarily correlate with malignancy [4,5]. In the case of pathophysiology, nabothian glands in the cervix are mainly responsible for mucus secretion. If the mucosa of the cervix covering these glands blocks the gland's opening, it may interfere with mucus secretion by the glands. When mucus accumulates in blocked glands, it forms smooth bulged lumps called nabothian cyst [5]. Mucinous retention cysts or epithelial cysts are multiple-opaque nodules (whitish to yellow) on the cervix. Chronic inflammation of the uterine cervix causes it. Nabothian cysts are typically tiny, seldom exceeding 4 cm in diameter [5,6]. They are frequently an incidental finding on clinical and pathological examinations of the uterine cervix [7].

Ultrasound examination is of value for detecting and diagnosing this kind of cysts. The necessity of treatment is to prevent pelvic inflammatory disease and Infertility. There are two steps for treating the disease: step one is using antibiotics in the acute phase, by which all sexual partners should be treated with the same antibiotic regime. Step two is electrocautery, heat, laser, and cryotherapy [8]. Cryotherapy is a common procedure to treat this disease. This device uses nitrous oxide (N_2O) and carbon dioxide (CO_2) to attain low temperatures to crystallize intracellular water, which eventually causes cell damage. This procedure can be performed without anesthesia, and in comparison, to other methods, it's cheaper and more accessible. There are some studies on the treatment of these kinds of cysts. Mary Seabury Stone studied the drainage of inclusion cysts (a kind of cyst in the vagina similar to a nabothian cyst in the cervix) by a small incision and evacuation of the component and destruction of the cyst wall [9]. This study compares the effect of uterine cervical Cryosurgery with drainage of nabothian cysts in chronic Cervicitis by syringe beside Cryosurgery.

Materials and Methods

Study setting:

A randomized clinical trial study was conducted between September 2016 to February 2017 in the GYN clinic in Jahrom city, Iran. The Ethics Committee Ethics Committee Ethics Committee Ethics Committee approved the study of Jahrom University of Medical Science (IR.JUMS.REC.1394.163), and the study protocol was registered with code of IRCT2016022821653N4.

Study population:

The formula $n = \frac{\left(z_1-\frac{a}{2}+z_1-\beta\right)^2(\delta_1^2+\delta_2^2)}{(\mu_1-\mu_2)^2}$ utilized for calculating the sample size, in which the power of study considered 80% and the confidence interval considered 95% ,α=0.05 , OR=3. 144 patients with chronic Cervicitis and nabothian cysts were randomly divided into two matched groups of 72 patients in experimental groups (drainage of nabothian cysts beside cryotherapy) and control group (cryotherapy alone).

Patient recruitment inclusion criteria were married women who had uterine cervical nabothian cyst with at least one child, recurrent pelvic infection (ICD-10 code N72), and Patients who have not responded to medical therapy. Nabothian cysts were diagnosed through physical examination or ultrasonography diagnosed cyst with a minimum size of 5 mm, and chronic Cervicitis was diagnosed through Pap smear).

A pelvic examination was done by a gynecologist using a speculum and endocervical and Vaginal discharge that was inserted on a slide with a sterile swab and checked for any cervicitis under the microscope if there was any infection that treated before cryotherapy through medical therapy. For all patients who have not improved after three treatments, uterine cervical discharges are sent to a laboratory for culture treatments; uterine cervical discharges are sent to the laboratory for culture. Then, we treat the patients based on the type of pathogens reported by a pathologist.

Subjects who had a history of vaginal bleeding, pregnant women, immune deficiency disease or autoimmune disease, other underlying diseases, and those who had not consent for cervical nabothian cysts drainage after explanation from the physician were not included. Subjects with definitive diagnosis or suspicion of genital cancers and positive Pap smear during the last month with detection of cervical dysplasia (pre-cancer), neoplasia, and malignancy were also not included. The Patients with missing follow-ups and who were not willing to continue the study were excluded.

We explained the reasons for this procedure for each patient in detail and obtained written consent from them.

Procedures:

The procedure and side effects were explained carefully for the patients; then a non-steroidal anti-inflammatory agent was prescribed 30 to 60 min before intervention (Preferably in the form of rectal suppositories) [10]. The patient was placed in the dorsal lithotomy position for a speculum examination. The Uterine cervix was brought into view; then vaginal preparation was performed by Betadine and (4*4) sterile gauze pads. All the nabothian cysts were evacuated using a 10cc syringe needle. Then, the large cysts are pressurized by ring forceps to ensure complete drainage of the nabothian cysts. A cryoprobe tip allowing the most effective freezing effect to 5 mm beyond the extent of nabothian cysts was chosen for each patient. A probe tip was placed inside the cervix, to cover the lesion entirely and refrain from contact with the vaginal walls. After that, the cryoprobe's handle was pulled outwards from the wall of the vagina and other tissues [11]. After the tip was secured, the device turned on and checked the tank pressure to ensure an adequate supply readies the device. A water-soluble gel or lubricant was applied to the tip of the cryoprobe. Cryotherapy with Crystallization of intracellular water eventually causes cell destruction and destroys the cervical epithelium. Intransitive temperature for cellular damage was in the range of -20 to -30 ° C. freeze-thaw-freeze method was used in our study in which by 3 minutes freezing was conducted to make an ice ball extending 5 mm beyond the cervical lesion. The freezing mechanism was then deactivated to allow for a 5 minutes thaw. The probe should not be actively loosened from the cervix but defrost and detach by itself. After thawing for 5 minutes, the lesion was refrozen for another 3 minutes [12]. Cervical epithelium was frozen to a depth of 6 to 10 mm. A follow-up sequence was discussed with the patient one month later. The first Pap test was delayed at least 3 months to complete healing.

Study variables:

Primary endpoint of this study was the patient's symptoms (Vaginal Bleeding, Abdominal pain, Dysuria, dyspareunia, vaginal discharge, frequent urination) and the procedure complications. Also, sociodemographic characteristics (age, Occupation, Educational level, Contraception method, number of pregnancies and history of previous surgery) were recorded to ensure matched groups. The main study outcome was the duration of courses till complete treatment.

Statistical analysis

SPSS statistical software, version 21, was used to analyze the data. Descriptive statistics were employed to evaluate complications between groups before and after the intervention to examine demographic data and reported as numbers with percentages or medians with range paired t-tests. After the intervention, a student t-test was performed to compare some of the variables between the two groups. Chi-square was used to investigate in Socio-demographic characteristics of participants in the control and experimental groups. McNamara's test was used to determine pre-post intervention changes in

symptoms. A P-value lower than 0.05 was considered significant.

Results and Discussion

One-hundred forty patients were recruited in the experimental section (n=70) and control (n=70) groups. The chi-square statistical tests showed no significant difference between the control and experimental groups in terms of the participants' ages, Occupation, educational level, Contraception method, number of pregnancies, and history of previous surgery Table 1.

Table 1: Sociodemographic variables in study participants

		Experimental		Control		P
		Mean/n	SD/%	Mean/n	SD/%	
Age, years	under 30	13	18.57	26	37.14	0.109
	30-34	26	37.14	21	30	
	35-39	13	18.57	10	14.29	
	40 and higher	18	25.71	13	18.57	
Occupation	Housekeeper	63	90	61	87.14	0.781
	Employee	4	5.71	7	10	
	Freelance	3	4.29	2	2.86	
Education level	Under diploma	44	62.86	35	50	0.354
	Diploma	17	24.29	21	30	
	Higher education	9	12.86	14	20	
Contraceptive method	Non	6	8.57	8	11.43	0.137
	Natural	52	74.29	48	68.57	
	Condom	9	12.86	6	8.57	
	Natural and condom	3	4.29	8	11.43	
History of previous surgery		19	26.4	17	23.6	0.786
Gravidity	1.00	1	1.43	2	2.86	0.196
	2-4	57	81.43	58	82.86	
	5-9	7	10	8	11.43	
	More than 9	2	2.86	0	0	
	Missing	3	4.29	2	2.86	
Parity	1	2	2.86	0	0	0.479
	2-4	13	18.57	9	12.86	
	More than 4	1	1.43	11	15.71	
	Missing	54	77.14	49	70	
Labor	1	1	1.43	0	0	0.657
	2-4	60	85.71	60	85.71	
	More than 4	5	7.14	5	7.14	
	Missing	4	5.71	5	7.14	
Abortion	None	57	81.43	64	91.43	0.231
	1	1	1.43	0	0	
	2-3	11	15.71	6	8.57	
	More than 3	1	1.43	0	0	

An exact McNamara's test determined a statistically significant difference in the proportion of vaginal bleeding occurrence and post-intervention in both experimental and control groups, showing a decreased in the symptom incidence<0.0001. Also, abdominal pain, dysuria, dyspareunia, vaginal discharge, and frequent urination occurrence decreased significantly post-intervention, p<0.0001. Both groups showed a significant decrease in symptoms incidence (Table 2).

There was a significant difference between the two groups in the duration of treatment (P=0.001) (Figure1). The mean duration of the treatment course in the experimental group was 5.4±1.59 months (minimum 1 to maximum 9); while it was 7.91±1.59 months in the control group, showing a statistically higher duration of treatment in the control group.

Table 2: Incidence of the symptoms before and after intervention

		Experimental		Z	P	Control		Z	P
		Count	%			Count	%		
Vaginal Bleeding	Before	68	97.14	-8.185	<0.0001	65	92.86	-8.062	<0.0001
	After	1	1.43			0	0		
Abdominal pain	Before	63	90	-7.874	<0.0001	38	54.29	-5.925	<0.0001
	After	1	1.43			1	1.43		
Dysuria	Before	67	95.71	-8.185	<0.0001	52	74.29	-7.211	<0.0001
	After	0	0			0	0		
Dyspareunia	Before	30	42.86	-5.477	<0.0001	29	41.43	-5.385	<0.0001
	After	0	0			0	0		
Vaginal discharge	Before	57	81.43	-7.55	<0.0001	37	52.86	-6	<0.0001
	After	0	0			0	0		
Frequent urination	Before	32	45.71	-5.657	<0.0001	26	37.14	-5.099	<0.0001
	After	0	0			0	0		

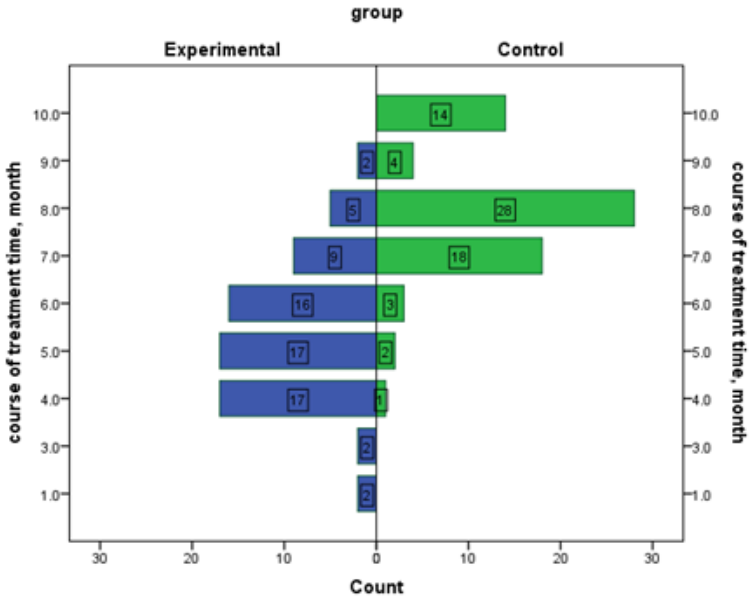

Figure 1: Duration of treatment in each group

As demonstrated in Table 3, in the linear regression of the study variables, none of the variables expect the groups significantly predict the duration of treatment, t=9.87, P=0.001.

Table 3: Linear regression of the study variables predicting duration of treatment

	Beta	T	P
group	0.66	9.78	0.001
Occupation	-1.14	-0.47	0.64
Education level	-0.10	1.43	0.16
age	-0.06	-0.34	0.74
Contraceptive method	0.04	0.47	0.64
Vaginal Bleeding	0.11	1.17	0.25
Abdominal pain	-0.16	-1.44	0.15
Dysuria	-0.03	-0.32	0.75
Dyspareunia	0.01	0.07	0.95
Vaginal discharge	0.15	0.90	0.37
Frequent urination	-1.14	-0.47	0.64

No adverse events were being reported in both groups.

The most frequent cysts are cervical cysts which are unfortunately poorly studied in pieces of literature. We have compared the effect of uterine cervical Cryosurgery (cryotherapy) with draining of nabothian cysts in chronic Cervicitis by syringe besides Cryosurgery. Our results showed that the second method, which is the combination of nabothian cysts drainage beside cryotherapy and medical therapy (antibiotics), is more effective. We did not find the comparison of these two methods in other researches, and there are much fewer studies focused on the drainage of nabothian cysts, so as a result, we applied a new method for the first time. The critical point is that all symptoms have improved significantly after intervention (Vaginal Bleeding, Dyspareunia, Frequent urination, abdominal pain, dysuria, and Vaginal discharge) in this method and the traditional method. According to our results, the duration of treatment in patients with nabothian cysts drainage besides cryotherapy decreased significantly. In the study of Fisun Vural et al., a woman who was 38 weeks pregnant arrived to the maternity unit with labor pain and a protruding cystic mass (big nabothian cyst) out of the vaginal canal, according to the study. A simple draining process was followed to reduce the cyst's size and facilitate vaginal birth. To limit the chance of cancer, they did a complete excision of the cyst [13]. Donald R. *et al*. used cervical cryotherapy to treat 75 patients with Cervicitis, and according to their results, healing was virtually complete in nearly all patients 8 weeks after freezing. They found out that Cryosurgery seems to have a place in treating Cervicitis [14]. B. ShilpaShivanna *et al*. in 2016 used Cryosurgery in the Management of Cervical erosion and concluded that Cryosurgery has 90% success rate. They also mentioned that this method is a simple, safe, effective & cheap treatment for cervical erosion [15]. Moawia E Hummeida *et al*. also revealed that cryotherapy is a safe procedure performed at all levels of health facilities, even remote areas, by trained mid-level health providers. And they have demonstrated that by combining cryotherapy with screening tests, most patients can be managed at the same visit in order, and most patients can be managed at the same visit in order. Most patients can be managed at the same visit to increase the efficacy of treatment and prevention programs [15]. In the above study, cryotherapy has been confirmed. It has been considered the first line of the study, especially the combination of cryotherapy with other screening tests, which is exactly what we've done. Authors in another study showed that cryotherapy would be more successful if performed without much delay [16]. The studies, as mentioned earlier, are compatible with our study.

Conclusions

We found that the novel approach of nabothian cyst drainage combined with cryotherapy is as practical as cryotherapy alone and that it takes less time to attain complete improvement. As a result, if this approach is used, the frequency of Cryosurgery may be reduced.

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Authors' contributions

Based on the recommendations of the International Committee of Medical Journal Editors, all authors met the criteria of authorship.

Ethical Approval

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Conflict of Interest

We have no conflicts of interest to disclose.

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