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Original Research

Treatment of uterine cervical ectopy with acupuncture and analysis of risk factors in the metaplastic process

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Summary

Objective: To evaluate acupuncture as a therapeutic method for uterine cervical ectopy with analysis of risk factors that interfere with the metaplastic response. *Materials and Methods:* From November 2010 to December 2015, the authors selected 51 healthy women with ectopy, reproductive age, no previous therapy, and negative conventional cytology Pap smear (CPS) for malignancy in the study group (S), treated with ten acupuncture sessions, weekly, and control group (C) with expectant management. The authors conducted anamnesis directed to Traditional Chinese Medicine (TCM), collection for liquid-based cytology (LBC), and colposcopy with photographs at study inclusion and follow-up at 90 days. The authors evaluated the therapeutic response by means of computerized planimetry in the images with 3% acetic acid solution (aa), considering the differential of the percentages of the areas of ectopy (ΔPe). The data were analyzed statistically. *Results:* Group S had 23 women and group C had 28. The mean age was 25.6 years, predominantly Caucasian, symptomatic, and non-smokers (100%). Group S presented a later age for first sexual intercourse ($p < 0.001$) and used less hormonal contraceptives ($p < 0.001$). LBC confirmed benignity and found no deviation of flora for bacterial vaginosis (BV). Group S presented higher ΔPe than C ($p < 0.001$). *Conclusions:* The authors observed a favorable therapeutic effect of acupuncture on the metaplastic process. The use of hormonal contraceptives and age of first sexual intercourse were the relevants risk factors, the same did not occur in smoking subjects and in the deviation of flora to BV.

Key words: Acupuncture; Ectopy; Treatment; Risk factors.

Introduction

The uterine cervix is covered by squamous epithelium in the ectocervix and by columnar epithelium in the endocervix. Ectopy is the presence of columnar epithelium on the ectocervix [1]. It is considered a physiological phenomenon originating in embryogenesis [2]. The squamous columnar junction may vary during female life by the influence of the sexual steroids [3]. It affects young women, reaching a prevalence of 17% to 50% of the cases [2].

Ectopy may be asymptomatic or cause mucorrhea, postcoital hemorrhage, recurrent cervicitis, dyspareunia, and pelvic pain [4]. Colposcopy is used to confirm the diagnosis. Re-epithelialization of the ectocervix occurs spontaneously, through metaplasia of the columnar epithelium triggered by the Ph vaginal acid. Influenced by hormonal stimulation, the process may extend for months or years [1]. For this reason, the treatment is currently controversial [2]. The risk factors involved in the persistence of ectopy are those that interfere with metaplasia such as BV, combined oral contraceptive (COC) use, and smoking [1, 5].

The presence of symptoms [2], association with *Chlamydia trachomatis* [6], HPV [5, 7-11], HIV [12, 13], and possible relation with cervical intraepithelial neoplasia [14] motivate the therapeutic intervention [2, 5]. In China, ectopy is commonly treated, since it is considered a common expression of chronic cervicitis [15].

Therapeutic options that present satisfactory responses [2] include electrocoagulation, cryocauterization, chemical methods, laser vaporization, and coagulation or resection with high frequency waveguides [3, 4, 15, 16] Adverse effects are secondary infection, hemorrhage, endocervical canal stenosis, cervical synechia, dysmenorrhea, and dystocia in labor [17, 18].

The use of TCM in Gynecology points to encouraging results in studies in premenstrual tension syndrome, dysmenorrhea, polycystic ovarian syndrome, menopausal syndrome, female infertility, and assisted fertilization [19-23].

For TCM, ectopy is the presence of moisture and heat, stagnant in the liver meridian (L), exteriorized by the cervix. The state of fullness of energy in L generates heat

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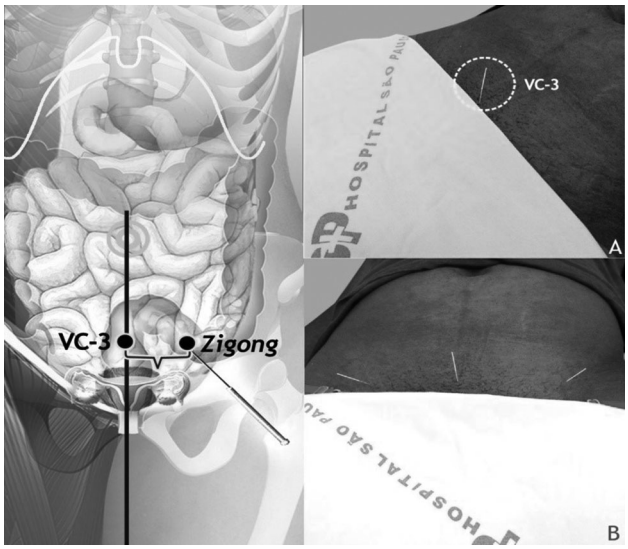

Figure 1. — Acupuncture points: VC3 or CV 3 (Zhongji) and M-TA-18 (Zigong).

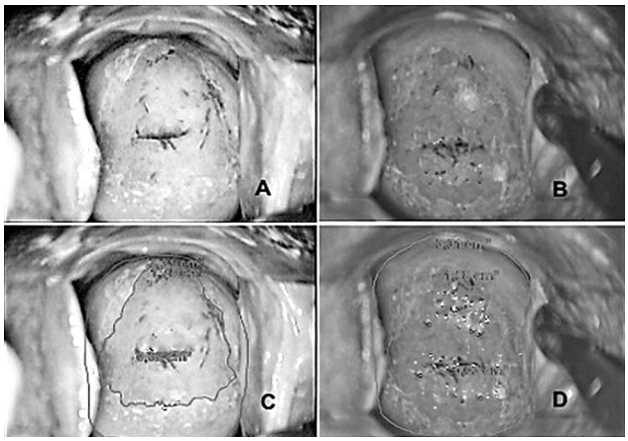

Figure 2. — Computerized planimetry. Photos A and C: initial planimetry using images with acetic acid 3%. Photos B and D: final planimetry.

and, by the Five-Motion Theory, affects the meridian of the spleen-pancreas (SP), accumulating moisture [24]. A recent study, based on this pathophysiology, used the Chinese herbal formulation Badushengjigao for the treatment of ectopy, in the presentation of vaginal suppositories, with favorable therapeutic results [24].

This study aims to evaluate the treatment of ectopy with acupuncture in healthy women and to analyze the risk factors involved in the metaplastic process.

Materials and Methods

From November 2010 to December 2015 the authors evaluated 51 healthy women in reproductive age, with ectopy confirmed by colposcopy, without previous treatment and negative CPS for malignancy. The authors do not include pretreated, pregnant, lactating, and immunosuppressed women in general. They randomized the groups in group S treated with acupuncture and group C under expectant management. The study was approved by the Ethics and Research Committee and the authors offered a free and informed consent form. After anamnesis contemplating TCM, the authors collected cervical samples for LBC in Thin Prep jars. The authors performed colposcopy in the inclusion and after a follow-up of 90 days, with image capture in jpeg format, by the Diagnose Pro 7.5 program.

Table 1. — *Epidemiological characteristics.*

Variable	Groups			
	Study	Control	Total	*p*
	n = 23	n =28	n =51	
Age (years)	27.4	24.1	25.6	0.04
Menarche (age)	12.3	12.2	12.2	0.977
First sexual intercourse	18.7	15.4	16.9	<0.001
Interval M/FSI	6.4	3.2	4.7	<0.001

Mann-Whitney: p = 0.05.; n = number of patients; M/C= menarche / first sexual intercourse.

S group received ten weekly sessions of acupuncture in specialized outpatient clinics of UNIFESP. The investigator answered all the cases using 25×40 mm disposable needles preceded by asepsis with cotton soaked in 70% alcohol, obeying the technique of unilateral insertion, manual manipulation until obtaining the *Te Qi* sensation with 20 minutes of permanence. The authors used the points: PC1 (*Tianchi*), LR5 (*Ligou*), GB30 (*Huantiao*), GB26 (*DaiMai*), SP4 (*Gongsun*), KL6 (*Zhaohai*), GB41 (*Linqi*), SP6 (*Sanyinjiao*), CV 3 (*Zhongji*), M-TA-18 (*Zigong*), BL32 (*Ciliao*), and ST40 (*Fenglong*) [25] (Figure 1).

The authors selected the photographs taken with 3% AA according to the following criteria: at least 75% of the visible ectocervical surface, visible cervical orifice, visible cervical curvature, and the best focus obtained for the identification of anatomical structures [13]. They adjusted the photographs for brightness, contrast, and sharpness.

The authors used the AxioVision LE 4.8.2.0 sp3 (08-2013) software for computerized planimetry, standardizing the scale in cm in each image, in order to obtain the total area of the cervix, external orifice, and ectopy area, which encompassed columnar and metaplastic epithelium [1, 8-15, 26, 27] (Figure 2).

They also considered for statistical analysis the difference of percentages of the areas of ectopy (ΔPe), resulting from the difference between the percentage of initial area (Pei) and final area (Pef). A reviewer (T.M), qualified in colposcopy, reviewed a sample of 10% of all the photos, which were analyzed using the Kappa statistical test for concordance analysis [1, 13]. In the statistical study, Mann-Whitney and Pearson's χ^2 tests were used for the epidemiological characteristics in the numerical and categorical variables, respectively. For the evolutionary analysis of the symptoms and results of the LBC, the authors used Fisher's Randomization test and in the analysis of the therapeutic response with acupuncture they applied the Student *t*-test for independent samples.

Results

Groups S and C included 23 and 28 women, respectively, totaling 51 patients. The numerical and categorical variables of the epidemiological characteristics are listed in Tables 1 and 2. The mean age was 25.6 years, being higher in

Table 2. — *Epidemiological characteristics.*

Variable		Group						
		Study		Control	Total			*p*
		n	(%)	n	(%)	n	(%)	
Parity	0 - 1	17	73.9	21	85	38	74.5	0.81*
	2 - 3	6	26.1	7	15	13	25.5	
	Total	23	100	28	100	51	100	
Partners	1 - 3	17	74	16	57.2	33	64.7	0.771*
	4 - 6	4	17.3	10	35.7	14	27.4	
	7 - 10	2	8.7	2	7.1	4		
	Total	23	100	28	100	51		
Sexual frequency	0	5	21.7	6	21.4	11	21	0.651**
	1 - 2	3	13.1	4	14.3	7	17	
	3 - 8	9	39.1	12	42.9	21	40	
	9 - 16	6	26.1	6	21.4	12	22	
	Total	23	100	28	100	51	100	
Ethnicity	Caucasian	13	56.5	23	82.1	36	70.6	0.082**
	Afro-descendant	9	39.1	5	17.9	14	27.5	
	Asian	1	4.4	0	0	1	2	
	Total	23	100	28	100	51	100	
Smoking	Yes	0	0	0	0	0	0	
	No	23	100	28	100	51	100	
	Total	23	100	28	100	51	100	
Hormonal contraceptive	Yes	13	56.5	28	100	41	80.4	<0.001**
	No	10	43.5	0	100	10	19.6	
	Total	23	100	28	100	51	100	
Symptoms	Yes	10	43.5	16	57.1	26	51	0.331**
	No	13	56.5	12	42.5	25	49	
	Total	23	100	28	100	51	100	

** Mann-Whitney: p = 0.05; ** χ^2 Pearson: p =0.05; n = number of patients.*

the group S ($p = 0.04$). In the same way, the authors observed a greater average age of first sexual intercourse in the S group (18.7 years, $p < 0.001$). In both groups menarche occurred on average at 12.2 years ($p = 0.977$) and parity from 0 to 3 deliveries ($p = 0.81$). The Caucasian ethnicity was predominant ($p = 0.082$), and no patient reported smoking. All women in group C used COC ($p < 0.001$).

In the sample, 51% of the women were symptomatic ($p = 0.331$), predominantly with discharge, pain, post-coital bleeding, and association of other symptoms. Out of the symptomatic patients, 60% in the S group reported improvement in the follow-up versus 75% in the C group ($p = 0.664$).

LBC results confirmed initial CPS data for negative / inflammatory reports, metaplastic or columnar epithelial representation, and vaginal flora deviation for BV ($p > 0.999$).

The authors evaluated acupuncture therapy by computerized planimetry. Prior analysis of concordance between examiners was significant ($p < 0.001$). Both groups had a decrease in ΔPe except for one patient in C group. Study group presented higher ΔPe (11.6%), compared to group C (4.06%) (p <0.001) (Table 3).

Discussion

Ectopy has a well-established natural history [2]. It is considered a physiological phenomenon, being object of research over its real nosological role. However, it may predispose to infections such as Chlamydia trachomatis [2, 7], HIV [13, 14], HPV 16 and 18 [4, 8-12], and may have a possible relation to the genesis of cervical cancer [28].

The treatment is controversial, indicated in cases of exuberant symptomatology [2].

The present sample was composed of Caucasian, nulliparous, and young women, with a mean age of 25.6 years, in agreement with the literature [1, 27], especially in this environment, where the mean age was 26 [5] and 28.7 years [29]. This fact draws attention to the persistence of ectopy, which may possibly result from a late diagnosis or reveal a tendency towards conservative behavior, since the absence of treatment was an inclusion criterion.

Patients presented on average menarche at age 12, first sexual intercourse at age 17, had one to four sexual partners, and monthly sexual frequency ranging from three to 16 intercourses.

No patient reported smoking, however the use of COC was more frequent in group C (p <0.001). The COCs, except medroxyprogesterone alone, have been associated with larger areas of ectopy [30], although other studies relate

Table 3. — *Therapeutic response of acupuncture.*

Group	n	Pei (%)	Pef (%)	ΔPe (%)	*p*
Study	23	41.97	30.91	11.06	<0.001
Control	28	32.11	28.04	4.06	
Total	51	36.55	29.34	7.22	

Student t-test for independent samples: p = 0.05; n: number of patients; Pei: initial percentage of ectopy; Pef: final percentage of ectopy; ΔPe: differential of the percentages of ectopy.

COC [1, 30] and smoking with accelerated metaplasia [1]. Most patients reported symptoms, sometimes combined, with predominance of discharge and dyspareunia, according to the literature.[2]

Alternative treatment with acupuncture is pioneering. It aims to insert ectopy as part of a set of signs and symptoms that define a pattern of organic imbalance, as well as publicize the technique beyond the border of the pain treatment where it is most used.

The present authors were also the first in their environment, following previous models, to use computerized planimetry, which is generally considered accurate [1, 8-15, 26, 27]. However, the difficulty related to the quality of the photos must be recognized and emphasized, as in previous studies [1, 11]. Variations of the cervix according to size, parity, anatomical position, menstrual cycle, as well as leucorrhoea, vaginal wall size, and projections, and cooperation and relaxation of the patient during colposcopy make it difficult to capture the image. Although the authors obeyed criteria in the choice of images, they can add the fact that the fine alterations of the epithelium already translate metaplasia [1]. Despite these considerations, the present results pointed to a favorable therapeutic effect of acupuncture. In S group, women had, on average, 41.97% Pei and finished the study, in three months, with 30.91%, with ΔPe of 11.06% versus 4.06% in relation to group C ($p < 0.001$).

The present results are close to previous observational study [1], where Pei was 39% and 8% at the end of the study, at 2.7 years, in which variations of progression and regression occurred in the maturity process. However, the present follow-up was shorter.

Neither smoking nor deviation of the flora for BV influenced the therapeutic response. In contrast, the authors observed a possible negative influence of the age of first sexual intercourse ($p < 0.001$) and COC ($p < 0.001$).

Acupuncture appeared to exert a favorable stimulus on the physiological reparative process, after analyzing the photos with a 3% that rendered the metaplastic epithelium white, resulting from the reversible coagulation of cytokeratins in the squamous epithelium.

The mechanisms of action of acupuncture on the reproductive system are briefly mediated by beta-endorphins acting on the hypothalamus-pituitary-adrenal axis and gonadal axis [20] and the resulting effects are multimodal by physiological pathways, through these neuroimmunoendocrinological pathways. However, studies of these mechanisms, despite the fact that the clinical and experimental studies present interesting and promising results, are still inconclusive [20-24].

The present prospective observational case control study points to a conservative horizon in relation to ectopy, in which alternative active behaviors can be offered to selected patients. The authors had a small number of cases, which encourages them to continue the investigation. They also recognize the difficulty in accepting acupuncture because of the lack of knowledge by multiple audiences, especially in gynecological disorders. Finally, they must consider their inability to evaluate the genetic influences on the reparative response as a limiting factor for any evaluation of assessment of ectopy treatment [1].

Conclusion

The authors observed favorable effects of treatment with acupuncture for ectopy on the physiological metaplastic process. The study showed the incidence of ectopy in young women, Caucasian, nulliparous, symptomatic with predominance of discharge, non-smokers, and users of COC. COC use and the age of first sexual intercourse were relevant risk factors in the therapeutic response.

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