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Research Article

Autologous Platelet Rich Plasma Therapy for Cervical Ectropion - A Case Series Study

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Abstract

Cervical ectropion is sometimes a debilitating condition, because of recurrent purulent vaginal discharge, post coital bleeding and pelvic pain. Autologous platelet rich plasma (PRP) is a regenerative treatment, which promote the natural healing. Here we have observed the treatment results of cervical ectropion. PRP treatment successfully induced the reepithelization of cervical ectropion and may become a non-invasive treatment option.

Keywords: *PRP; Cervical Erosion; Cervicitis; Regenerative Medicine; Cervical Reepithelization; Cervical Ectropion*

Abbreviations

PRP: Platelet Rich Plasma; PPP: Platelet Poor Plasma; CE: Cervical Erosion; HPV: Human Papilloma Virus; LEEP: Loop Electrosurgical Excision Procedure

Introduction

Autologous platelet rich plasma (PRP) is the processed liquid fraction of autologous peripheral blood with a platelet concentration above the baseline [1]. PRP use has increased in diverse medical fields, including gynecology. The mechanism of PRP treatment is using active factors (growth factors, cytokines) and adhesion proteins that are responsible for initiating the hemostatic cascade, synthesis of new connective tissue, revascularization, and mesenchymal stem cell trophic effect locally [2]. Main advantage of PRP include its safety and the ingenious preparation techniques of current commercial devices to prepare a biologic that can be used in broad application profile [3].

Cervical ectropion is commonly recognized as being physiologic condition caused by columnar epithelium from the cervical canal extending into the columnar portion of the cervix [4]. The prevalence is cervical ectropion ranges from 17% to 50% [4,5]. It may occur in adolescence, during pregnancy or response to hormonal contraception [6,7]. Common symptoms include mucopurulent vaginal discharge, postcoital bleeding, recurrent cervicitis, and pelvic pain [7]. Other common cause of cervical ectropion is chronic cervicitis, which

predisposes women for HPV, HIV infection and cervical cancer [8]. The common etiologies include infections such as *Chlamydia, Gonorrhea, Trichomonas vaginalis*, viral infections HSV and HPV [9]. Allergies and irritation by chemical or physical like intrauterine device, contraceptive diaphragm, condom, tampon, douches, wash, spermicidal childbirth, and D&C procedure [10].

Cervical ectropion is treated by electric coagulation [7], cryotherapy [11-14], microwave coagulation [15], laser therapy [16]. However, each treatment has adverse effects, commonly surgical bleeding, abundant vaginal discharge after surgery, scar formation [17]. Approximately 1- 2% of the patients may experience postoperative hemorrhage acquiring hospital admission and re-coagulation. Hua X., *et al*. have introduced the PRP gel to cervical erosion [17], showing the 93.7% cure rate. Jain S., *et al*. used the PRP injection for chronic cervicitis and the cure rate was 76.67% [18].

Aim of the Study

In this case series study, we aimed to determine the cure rate of cervical ectopy using PRP injection in T zone.

Materials and Methods

A case series study was conducted in Gynecology department of MD health care center from April 1, 2021, to April 1, 2022, due to ethical consideration, written and informed consent was taken from each Patient after explaining the procedure in detail its beneficial outcome and side effects. Specific infection was investigated using cervical swab PCR. Women found to have cervicitis were provided a course of oral and vaginal antibiotics and those who were not responsive to antibiotic treatment were enrolled in the study. The inclusion criteria were the following symptoms: vaginal discharge, postcoital bleeding, pelvic pain, recurrent cervicitis. Exclusion criteria were platelet dysfunction, prolapse uteri, major medical illness, post-menopausal and precancerous state. After proper history, routine pelvic examination and colposcopy, pap smear was done to 25 women of 25 - 40 yrs.

10 ml of whole blood was collected by venipuncture in a preloaded anticoagulant syringe and processed by density dependent separation, first centrifugation at a speed [1000 rpm] for 15 minutes to settle the RBCs in the lower part with buffy coat and plasma containing platelets. Subsequently the supernatant was transferred into the other sterile tube for centrifugation at a higher speed [1500 rpm] for 5 minutes to obtain platelets concentrate. Upper 2/3 was discarded as a Platelet Poor Plasma (PPP) zone and lower 1/3 is PRP with platelets at the bottom of the tube. The concentrated platelets palate with 3-5 ml of plasma was mixed homogenously and injected within 30 minutes under sterile conditions with 26G needle precisely in the targeted area at more than 10 sites into intra and peri-cervical tissue in each assigned patients of CE. Three sittings were given 1 to 2 weeks interval. Patients were instructed for regular follow up first within 30 days, then 3, 6 months interval. Follow-up includes subjective assessment of symptoms, clinical examination, colposcopy, and PAP smear if needed. It was a day care nonsurgical procedure.

The colposcopy was done at x5 magnification in every patient. The colposcopy image was processed using image J program. If the ectropion size reduced less than 1 cm diameter, considered as cure.

Results and Discussion

In this study we found that patient treated with PRP showed good relief in symptoms and no recurrence. Our analysis showed following results. Table 1 mean age of patients suffering from CE was 30.2 ± 4.9 years in both the groups. 35.3% (n = 6) was para, 64.7% (n = 14) was null parous. Contraceptive methods were condom 70.6% (n = 12), IUD 17.6% (n = 3), combined oral contraceptive 5.9% (n = 1), implant usage 5.9% (n = 1). Patients vaginal condition was 71.4% (n = 10) had bacterial vaginosis, 28.5% (n = 4) had candidiasis, normal vaginal flora 17.6% (n = 3). Patients 29.4% (n = 5) had *Gardnerella vaginalis*, *Ureaplasma* infection 23.5% (n = 4), *Mycoplasma* infection 11.8% (n = 2). Totally, 17 patients received antibiotic treatment as per Sanford guideline. No cure was seen after antibiotic treatment.

	Baseline patient characteristics	Mean ± SD
1	Age	30.2 ± 4.9
2	Parous vs non parous	35.3% (n = 6) 64.7% (n = 14)
3	**Contraceptives**	
	Condoms	70.6% (n = 12)
	IUD	17.6% (n = 3)
	Combined oral contraceptive	5.9% (n = 1)
	Implant	5.9% (n = 1)
4	**Vaginal condition**	
	Normal vaginal flora	17.6% (n = 3)
	Bacterial vaginosis	71.4% (n = 10)
	Candidiasis	28.5% (n = 4)
5	**Cervical PCR**	
	Gardnerella vaginalis	29.4% (n = 5)
	Ureaplasma	23.5% (n = 4)
	Mycoplasma	11.8% (n = 2)
6	**Symptom**	
	Vaginal discharge	90.9% (n = 20)
	Postcoital bleeding	29.4% (n = 5)
	Pelvic pain	17.6% (n = 3)
	Recurrent cervicitis	90.9% (n = 20)

Table 1: *Patients' characteristics.*

The PRP characteristics is shown in table 2. The platelet was concentration from 253.6 x 10^3/mm^3 to 2642.2 x 10^3/mm^3, which is 11.03 times concentrated after the collection of PRP. Totally 5 ml liquid PRP was injected in cervical transition zone. The main symptoms during injection were pain (45.5%) and bleeding (90.9%) at injection site. However, both symptoms relieved after the procedure.

The cure rate of PRP treatment for CE was 82% (Figure 1). Reepithelization time was 9.5 ± 3.04 weeks (Table 3). Bleeding after treatment was 9%, but the amount was little. No significant adverse effect was found after 3 months. 2 patients had recurrence of CE, 4 weeks later. These patients were HPV positive.

Cervical ectropion is common condition mostly asymptomatic but sometimes devastating vaginal discharge. In Mongolia, in most cervical ectropion cases a treated using Loop or Ball Electrocoagulation, which is effective but tissue damage and cervical scarring forms the cervical stenosis. The incidence rate of stenosis after loop electrosurgical Excision Procedure (LEEP) is 1.3 to 19%, post laser conization 3 - 25% [19-25].

Cervical ectropion increases the vulnerability of acquiring sexually transmitted infections, including *chlamydia*, *gonorrhea* and HIV [26]. Cervical microbial study showed the high rate of bacterial vaginosis and candidiasis. Moreover, *Mycoplasma* and *Ureaplasma* infec-

№	Category	PRP characteristics	Response
1	Preparation of PRP	Initial blood volume (ml)	10
		Anticoagulant (type)	Sodium citrate
		System (open/closed)	Open
		Centrifugation (yes/no)	Yes
		Number	1
		Speed (rpm)	1000 rpm, 15 min
			1500 rpm, 5 min
		Final PRP volume (mL)	3 - 5
2	Characteristics of PRP	Mean platelet volume (fL) before	Platelets: 253.6 x 10^3/mm^3 (10^9/L)
		Activation	Endogenous
		Final Platelet concentration increase	x 11.03
3	Application characteristics	Formulation type (liquid, gel, scaffold)	Liquid
		Administration route (under colposcopic magnification)	Experienced gynecologist under by an 26G needle to transformation zone
		Dosage (no. of applications and interval)	Total of 3 injections at weekly intervals
		PRP volume (ml)	5
		Dose number of injected platelets (10^3/mm^3)	Platelets: 2642.2 x 10^3/mm^3 (10^9/L)
		Tissue	Uterine cervix
		Pathology	Cervical ectropion
4	Other remarkable PRP and study features	e.g. Further data about preparation, activation, quantification, application, combination with other products (i.e. Anesthetics, others), fresh-frozen	Fresh PRP, no anesthetics
5	Sensations, during injections, No. (%)	Serious adverse events	0% (0/22)
		Cervical pain	45.5% (10/22)
		Cervical swelling	0% (0/22)
		Injection site bleeding	90.9% (20/22)

Table 2: *Summary of PRP characteristics based on reporting recommendations.*

	Category	PRP injection 3 times later	Response
1	Epithelization time	9.5 ± 3.04 weeks	82%
2	Symptom relief	Vaginal discharge	75% (15/20)
		Postcoital bleeding	100% (5/5)
		Pelvic pain	100% (3/3)
		Recurrent cervicitis	90% (18/20)
3	Adverse events, following injections, No. (%)	Serious adverse events	0% (0/22)
		Cervical bleeding	9% (2/22)
		Injection site pain/bruising	0% (0/22)
4	Adverse events, 3 months, No. (%)	Serious adverse events	0% (0/22)
		Cervical bleeding	0% (0/22)
		Injection site pain/bruising	0% (0/22)
5	Recurrence of CE		2/22

Table 3: *Treatment results and adverse events, recurrence rate.*

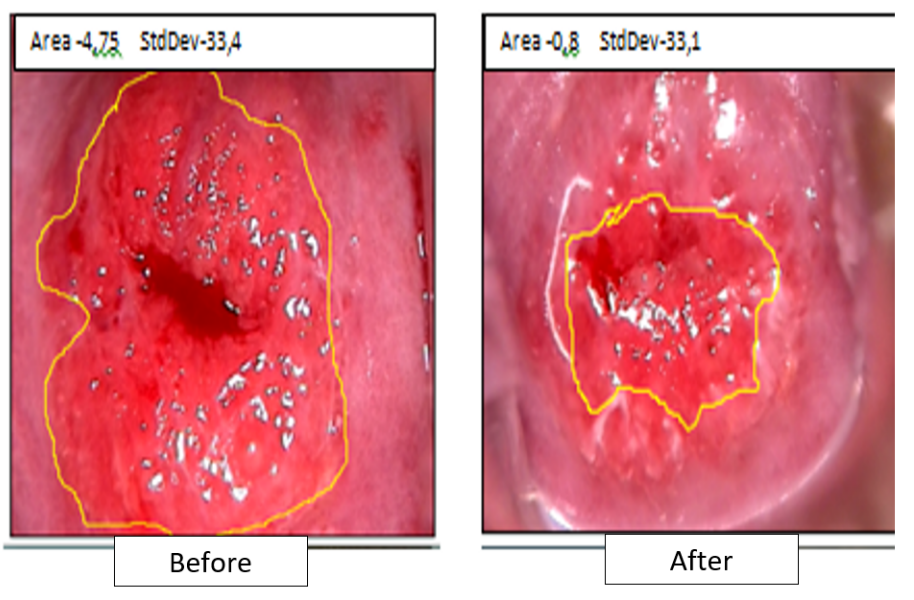

Figure 1: *Colposcopic findings and image J analysis.*

tion was higher than general population in Mongolia. However, even after the antibiotic treatment none of the CE cases cured. On the other hand, cervical metaplasia the process of squamous cell replication and differentiation leads to favorable ground for HPV 16 infection [27]. In current study 2 patients with HPV infection had recurrence of CE.

The treatment goal for symptomatic ectropion is to destroy the glandular columnar epithelium, thereby inducing squamous metaplasia, leading to resolution of vulvovaginal discharge, irritation, yellowish discharge, and dyspareunia [28].

Platelet-rich plasma is a promising treatment which promotes the natural healing. PRP is currently characterized by its absolute platelet concertation, which should be 1 x 10^6/μL or an approximately five-fold increase in platelets from baseline [29]. Previous studies using PRP for cervical ectropion and cervicitis showed high cure rate and low complication rate [17,18].

Furthermore, PRP treatment ensured complete preservation of the physical characteristics (e.g. the elasticity) and physiologic function and repairing of fibrose tissue, cure of deep-seated infection and inflammation. Other studies also found the PRP plays an important role regeneration of inflamed, fibrosed epithelial tissue of cervix [29]. Recurrence of cervical ectropion post treatment observed in 2 cases with HPV infection. Thus, further investigation with recurrence is needed.

Conclusion

Autologous PRP treatment may become first line treatment for cervical ectropion. The treatment was effective, showing epithelization in short time, without complication. Further large clinical study with control needed to confirm the PRP in large study population.

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Conflict of Interest

There is no conflict of interest exists.

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