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Effect of Platelet-Rich Plasma in Treatment of Cervical Ectopy

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Abstract

Ectopy occurs when the columnar epithelium of the endocervical canal extends outwards into the ectocervix, which is normally covered by stratified squamous epithelium. Platelet-rich plasma (PRP) is an innovative treatment designed to stimulate cellular regeneration, neovascularisation, and healthy cell formation. To study the effectiveness and efficacy of PRP in the treatment of patients with chronic cervicitis. This was a prospective cohort study, was carried out at the gynaecology department of Al-Zahraa University Hospital on 200 females having symptomatic cervical ectopy. Full history taking and examination, PAP smear, colposcopy examination, preparation and application of Platelet-rich plasma (PRP) gel, and follow-up visits with colposcopic assessments. The patient is positioned in a lithotomy position for the examination and PRP application, advised to avoid sexual intercourse and vaginal douching for a month, and the procedure is repeated again after 7 days. The follow-up visits are conducted after 1st, 4th and 12th weeks after treatments. There was high statistically significant difference between cured and non-cured patients as regard presence of irregular vessels during colposcopic examination by green filter ($P<0.0001$). There was significant positive correlation between contact bleeding, Nabothian cyst, ectopy and endocervical hyperplasia with time of cure ($P = 0.023$, 0.038, 0.011 and 0.018 respectively). Conclusion: PRP may become the treatment of choice for symptomatic cervical ectopy but long-term evaluations and large randomized controlled trials are needed.

Keyword: Adverse effect; Cervical ectopy; Laser treatment; Platelet-rich plasma; Therapeutic effect

1. Introduction

Cervical ectopy may be categorized as either physiological or pathologic. Physiological columnar ectopy results when the squamous epithelium of the cervix is replaced by columnar epithelium. In contrast, pathologic ectopy manifests as tissue that is red, granular and papillary in appearance. Cervical ectopy can be associated with chronic or recurrent symptoms of cervicitis like leucorrhea, vaginal itching, pruritus, dyspareunia, pelvic pain, and post-coital bleeding [1].

The prevalence reported for cervical ectopy ranges from 17% to 50% [2]. It may occur

in adolescence, during pregnancy, or in response to hormonal contraception [3].
Treatment options include electrocoagulation, laser therapy and cryocautery. With those treatments, surface damage is often seen, which induces bleeding and possible cervix scarring stenosis [4].
Platelet-rich plasma (PRP) is more popular as a nonoperative treatment option for a broad spectrum of medical disorders [5].
Autologous PRP is derived from an individual's whole blood then centrifuged to remove red blood cells. The remnant plasma has a five to ten folds higher concentration of growth factors than whole blood. These growth factors have been found to promote natural healing responses by researchers across multiple specialties, such as dermatology, dentistry, urology, and gynecology [6].
There is a real possibility that PRP treatment will be widely used for cervical ectopy because of its ease, affordability (it costs about 20% less than laser treatment), and effectiveness [7].
The aim of Work was to study the effectiveness and efficacy of PRP in treatment patients with chronic cervicitis

2. Patients and Methods

This was a prospective cohort study that was conducted at the gynecology department of Al-Zahraa University Hospital on 200 females having symptomatic cervical ectopy after obtaining consent from them to participate in this study, and the study protocol was approved by the ethical committee.

2.1 The inclusion criteria

Age more than 21 years, patients have symptoms of: vaginal discharge, postcoital bleeding, pelvic pain, and recurrent cervicitis, cervical ectopy appearing as reddish granulation tissue raised above the surrounding and surface with examination by colposcopy.

2.2 The Exclusion criteria

Age less than 21 years, other gynecologic disorders, pregnancy or breastfeeding, patients had previous history of electrocautery or laser therapy for cervical ectropion, patients with cervical intraepithelial neoplasia, patients with immunocompromised conditions (i.e., diabetes mellitus, immunodeficiency syndromes) and use of corticosteroid or immunosuppressive drugs and patients having hormonal contraception

2.3 Methods

All patients had been subjected to:

2.3.1 Full history taking

the menstrual history, previous obstetric history, contraceptive pills, medical and surgical history.

2.3.2 Thorough clinical examination

visual vaginal examination to exclude any other local lesion or gynecological disorders.

2.3.3 PAP smear

All patients had been undergoing smear tests to exclude the presence of any dysplastic or neoplastic cells.

2.3.4 Colposcopy examination

Patient positioned in a lithotomy position and cervix will be washed by saline solution then Solutions of acetic acid and lugol`s iodine will be applied to the cervix.

2.3.5 PRP preparation

(1) venous blood (15–25 mL) will be drawn from the patient's arm in anticoagulant-containing tube; (2) The blood will be centrifuged twice at 1500 rpm for 10 minutes and 8 to 10 mL of PRP will be extracted. The PRP concentrate is divided

into 2 portions of 4 to 5 mL each, to be used in 2 applications. One used immediately and the other stored at −30 °C and will be applied a week later to the patient in the same manner.

2.3.6 PRP application

Three to seven days after end of a menstrual flow, Before the procedure, 0.8 mL of a 10% solution of calcium chloride with 800 units of thrombin was added to the PRP concentrate to activate the platelets and the resulting gel was loaded into a special application device Patients positioned in a lithotomy position, with their cervix will be disinfected and exposed by a speculum then the surface of the cervical erosion will be covered with PRP gel. The patient remains in the sitting lithotomy position for 15 minutes to maintain the PRP gel on the cervical surface. This manner was applied after 7 days.

The patient's returns home on the day of treatment and advised to avoid sexual intercourse and vaginal douching for a month.

2.3.7 Follow-up visits

conducted after the end of the 1st, 4th and 12th week after treatments. All patients undergo a colposcopic assessment at each visit. Failure of treatment for cervical ectopy would occur if the abnormal cells persist or return after a treatment has been performed.

3. Results

As shown in Table .1, the age of the patients with a mean value of 31.3 ± 4.74 years. The parity with a mean value of 2.62 ± 1.13 and a median value of 3. And regarding the mode of delivery, there were 95 (48%) patients with vaginal delivery and 104 (52%) patients with CS.

As shown in Table .2, the most presentation of symptoms was vaginal discharge occurred in 126 (63%) patients, contact bleeding occurred in 56 (28%) patients, Low back pain occurred in 54 (27%) patients and recurrent infection occurred in 44 (22%) patients.

As shown in Table .3 during vaginal examination by speculum, 44 (22%) patients were hypertrophic, 40 (20%) patients had Nabothian cyst, and 200 (100%) patients had ectopy.

As shown in Table .4, PAP smear results vary from Endocervical hyperplasia (7%), and the most common pathological findings were Chronic cervicitis (78%) and Negative for intraepithelial lesion or malignancy (NILM) (72%).

As shown in Table .5 the cure rate of symptoms in all studied patients, regarding low back pain and recurrent infection, all patients were cured, as regards vaginal discharge (85.7%) of patients were cured, as regards contact bleeding (89.3%) of patients were cured. As shown in table 6 the time of cure was (9%) of patients cured in the 1st week, 84 (42%) of patients cured in the 4th week while 182 (91 %) of patients cured in the 12th week and according to symptoms vaginal discharge was the first symptoms that have been cured then postcoital bleeding. As shown in table 7 there was a high statistically significant difference between cured and non-cured patients as regards age, smoking and mode of delivery (patients had vaginal delivery are higher in non-cure rate). There was a high statistically significant difference between cured and non-cured patients as regards the presence of irregular vessels during colposcopic examination by green filter. There was no significant difference between the cured and non-cured patients as regards parity, contraceptive methods. As shown in Table .8, there was a significant positive correlation between contact bleeding, Nabothian cyst, ectopy and endocervical hyperplasia with time of cure.

Table 1: Patients' characteristics in all studied patients

		Patients (n = 200)
Age (years)	Mean ± SD	31.3 ± 4.74
	Range	21-42
Parity	Mean ± SD	2.62 ± 1.13
	Median	3
	Range	1-5
Mode of delivery	Vaginal delivery	96 (48%)
	CS	104 (52%)

CS: cesarean section

Table 2: Symptoms in all patients studied

Symptoms	Patients (n = 200)
Vaginal discharge	126 (63%)
Contact bleeding	56 (28%)
Low back pain	54 (27%)
Recurrent infection	44 (22%)

Table 3: Vaginal examination by speculum in all studied patients

Vaginal examination	Patients (n = 200)
Hypertrophic	44 (22%)
Nabothian cyst	40 (20%)
Ectopy	200 (100%)

Table 4: PAP smear results of all studied patients

PAP Smear	Patients (n = 200)
Chronic cervicitis	156 (78%)
Negative for intraepithelial lesion or malignancy (NILM)	144 (72%)
Endocervical hyperplasia	14 (7%)

Table 5: Cure rate of Symptoms in all patients studied

Symptoms	Patients (n = 200)	Cured
Vaginal discharge	126	108 (85.7%)
Contact bleeding	56	50 (89.3%)
Low back pain	54	54 (100%)
Recurrent infection	44	44 (100%)

Table 6: Follow-up with the time of cure of the studied patients

	Patients (n = 200)	
Time	1st week	18 (9%)
	4th week	84 (42%)
	12th week	182 (91%)

Table 7: Difference between the cured and non-cured patients.

Patients (n=200)			Cured n=182 (91%)	Non-cured n= 18 (9%)	P value
Age (years)	Mean ± SD		29.3 ± 3.85	33 ± 4.21	0.0002*
	Range		21-39	25-42	
Parity	Mean ± SD		2.9 ± 1.2	3.2 ± 1.7	0.332
	Range		1-4	1-5	
Contraceptive methods	No		56(30%)	4 (22%)	0.058
	IUD		39(21%)	9 (50 %)	
	Coitus interruptus		42(23%)	2 (11%)	
	Safe period		45(25%)	3 (17 %)	
Mode of delivery	Vaginal delivery		81(44.5%)	15(83%)	0.002*
	CS		101(55.5%)	3(17%)	
Socio-economic status	Smoking	Yes	5 (2.75%)	6(33%)	< 0.001*
		No	177(97.25%)	12(67%)	
	Number of partners		1-3	1-3	----
Colposcopic examination Green filter (irregular vessels)			Yes (27%)	Yes (100%)	< 0.0001*

Table 8: Correlation between different parameters and time of cure.

	r	P. Value
Symptoms		
• Vaginal discharge	0.323	0.625
• Contact bleeding	0.874	0.023*
• Low back pain	0.152	0.736
• Recurrent infection	0.258	0.425
Vaginal examination		
• Hypertrophic	0.576	0.064
• Nabothian cyst	0.766	0.038*
• Ectopy	0.934	0.011*
PAP Smear		
• Chronic cervicitis	0.698	0.071
• Endocervical hyperplasia	0.881	0.018*

4. Discussion

Cervical ectopy is considered to be a physiological condition caused by extending columnar epithelium from the cervical canal into the vaginal portion of the cervix. The prevalence reported for cervical ectopy ranges from 17% to 50%. It may occur in adolescence, during pregnancy, or in response to hormonal contraception [8].

In recent years, autologous PRP has received more and more attention in the fields of orthopedics, dentistry, dermatology, ophthalmology, and cosmetic surgery. PRP contains multiple growth factors that greatly promote tissue healing by enhancing cellular chemotaxis, the removal of tissue debris, cell proliferation and differentiation, angiogenesis, and the laying down of extracellular matrix [9].

In the current study we found that the mean age of the patients was 31.3 ± 4.74 years. The mean parity was 2.62 ± 1.13 and a median value 3. And regarding the mode of delivery, there were 95 (48%) patients had a vaginal delivery and 104 (52%) patients had CS.

Hua et al., [7] showed that the mean age of the patients was 35.1±4.39 years. The mean parity was 1.15±0.44. There was no significant difference between groups regarding age and parity.

In the present study we found that the most presentation of symptoms was vaginal discharge occurred in 126 (63%) patients, contact bleeding occurred in 56 (28%) patients, Low back pain occurred in 54 (27%) patients and recurrent infection occurred in 44 (22%) patients.

A similar result was reported by Aitah et al. [9] who stated that the majority of PRP and silver nitrate groups (74 and 66%, respectively) had discharge; both groups were non-significantly different in the presence of discharge (P=00.383). The majority of PRP and silver nitrate groups (92% and 88%, respectively) did not develop bleeding; both groups didn`t has a significant difference in the incidence of bleeding.

In the present study during cervical examination by speculum, 200 (100%) patients included in the study had cervical ectopy, 44 (22%) of those patients had hypertrophic cervix and 40 (20%) of patients had Nabothian cyst.

Our findings regarding PAP smear clearly revealed that results vary from Endocervical hyperplasia (7%) and the most common pathological finding was Chronic cervicitis (78%) and Negative for intraepithelial lesion or malignancy (NILM) (72%).

Junior et al.,[10] reported that atypical PAP smears were more frequent in the ectopy group than in the control group, and they were generally independent of age and the extension of ectopy. A localized immunodeficiency has been hypothesized to appear and depress the immunosurveillance and cell-mediated response in ectropion.

Regarding the cure rate of symptoms, all patients were cured from low back pain and recurrent infection, (85.7%) of patients were cured from vaginal discharge, (89.3%) of patients were cured from contact bleeding.

Hua et al., [7] conducted a randomized study to compare the effectiveness of autologous PRP application to that of laser treatment for cervical ectopy. They applied PRP twice on the cervical ectopy with a 1-week interval in 60 patients, while laser was used in other 60 patients.

They found that complete cure rate was 93.7% in the PRP group and 92.4% in the laser group ($p > 0.05$). The mean time to re-epithelialization was significantly shorter in the PRP group ($p < 0.01$). The rate of side treatment effects (i.e., vaginal discharge or vaginal bleeding) was much lower in the PRP group than in the laser group ($p < 0.01$). They concluded that PRP application appeared promising for the treatment of symptomatic cervical ectopy, as it resulted

in a shorter tissue healing time and milder side effects than laser treatment.

Our results regarding follow up clearly revealed that (9%) of patients were cured in the 1st week, 84 (42%) of patients were cured in the 4th week while 182 (91 %) of patients cured in the 12th week and according to symptoms vaginal discharge was the first symptoms that have been cured then postcoital bleeding.

Hua et al., [7] reported that 59 patients (93.7%) in the PRP and 60 (92.4%) in the laser group were free of symptoms, and the difference between the rates was not significant (P>0.05). During the follow-up vaginal discharge was observed in 25 patients in the PRP group, but the discharge was less profuse and of shorter duration than in the laser group. With laser treatment nearly all patients experienced a vaginal discharge as a reaction to treatment. There were 11 cases of mild bleeding that stopped on its own after a week. In the laser group, however, there were 25 cases of vaginal bleeding, including 2 cases of heavy bleeding that required treatment by vaginal tamponade. Besides, one patient in this group was treated with an oral antibiotic because of a foul-smell discharge.

This research was compared with a study performed by Jain et al. [11] to evaluate post-treatment symptom alleviation and repair of the damaged cervix in patients receiving conventional therapy (CT) or PRP therapy to treat chronic cervicitis as well as ectopy. The average age of patients with chronic cervicitis in both groups was 32–34 years. They also discovered development of vaginal discharge in both groups. In the PRP group, the entire patients were treated for postcoital bleeding, while in the CT group, only half of the patients were treated. 90% of individuals with dyspareunia improved after 6 months of PRP treatment.

Agah et al. [12] illustrated that in the PRP treatment group, 76.6% of patients were fully cured compared with 48.33% in the traditional group. Post-PRP results for a patient with a badly damaged cervix were encouraging, with a fully repaired cervical epithelium.

Bielecki et al.,[13] also discovered that PRP inhibited Staph. aureus and was active to encounter Escherichia coli, which explains why the treated group had less cervix discharge.

In the current study we found that there was a high statistically significant difference between cured and non-cured patients as regard age, smoking and mode of delivery (patients had vaginal delivery are higher in non-cure rate). There was a high statistically significant difference between cured and non-cured patients as regard presence of irregular vessels during colposcopic examination by green filter. There was no significant difference between cured and non-cured patients as regard parity, contraceptive methods.

Aitah et al.,[9] reported that there was no significant difference between cured and non-cured groups regarding age (P=0.190), the parity (p=0.459) and cervical erosion size at baseline follow-up at 4-, 8-, and 12-weeks post treatment (P=0.896, 0.605, 0.371, and 0.121, respectively).

In contrast, Wright et al. [14] documented that multiple logistic regressing analysis was used to predict the probability that a woman would have cervical ectopy. The predictor variables were woman’s age, parity, and history of using of hormonal contraceptives, presence of abnormal vaginal bleeding and presence of vaginal discharge.

5. Conclusion

In conclusion, the result of the present study indicates that PRP may become the treatment of choice for symptomatic cervical ectopy, but long-term evaluations and large randomized controlled trials are needed.

Conflict of interest:

no conflicts of interest.

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