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INTRAVESICAL INJECTIONS OF PLATELET-RICH PLASMA (PRP) IN TREATMENT OF INTERSTITIAL CYSTITIS REFRACTORY TO CONVENTIONAL TREATMENT – A PILOT STUDY

Hypothesis / aims of study
Interstitial cystitis/painful bladder syndrome (IC/PBS) is a debilitating chronic disease of unknown etiology characterized by urgency frequency and suprapubic pain at full bladder. Current treatments are usually unsuccessful in completely eradicating bladder pain and increasing bladder capacity. Autologous platelet-rich plasma (PRP) is growing in popularity as a therapy to augment wound healing, speed the recovery from muscle and joint injuries, and enhance recovery after surgical repair. PRP is extremely rich in growth factors and cytokines, which regulate tissue reconstruction and has been studied extensively among trauma patients and trauma experimental models. Tissue regeneration can be improved by local application of autologous bone marrow derived progenitor cells and PRP.

Study design, materials and methods
This pilot study attempts to use autologous PRP in treatment of interstitial cystitis refractory to currently available medical treatment or intravesical therapy. The results of this study might provide clinical evidence for a novel therapeutic regimen in the treatment of IC/PBS. A total of 17 patients with IC/PBS who have failed conventional treatments for at least 6 months was enrolled in this study. All patients had IC symptoms and proven to have diffused glomerulations after cystoscopic hydrodistention (HD) within recent 1 year without Hunner's lesion. The patients received intravesical injection of 10-12 mL PRP (extracted from 50ml of patient's own whole blood) followed by cystoscopic hydrodistention under intravenous general anesthesia in the operation room. The procedure was repeated every one month for a total of four treatments. Urine samples (30 mL) were also collected before intravesical PRP injection and at 4 weeks after each PRP injection. Primary end-point was the change of the O'Leary-Sant symptom score (OSS, including ICSI and ICPI) from baseline to 1 month after the last injection. Secondary endpoints include VAS, daily frequency, nocturia and functional bladder capacity (FBC) as record in 3-day voiding diary, Qmax, vided volume, post-void residual (PVR) and global response assessment (GRA). Urine samples were collected for urinary vascular endothelial growth factor (VEGF) and cytokines tests.

Results
Among the patients, 13 women completed the study. The mean age was 52.9±12.1 years (38-76). Table 1 shows the changes of symptom scores and urodynamic parameters. A significant improvement was noted in OSS after two PRP injections, in VAS after one and three PRP injections, in FBC after two and three PRP injections, and in GRA after each PRP injection. However, the improvement of the measures was not stable. At 1 month after four injections, the symptoms relapsed and bladder capacity decreased. Urinary interleukin (IL)-2 and IL-8 showed significant increase after the first PRP injection. In patients with VAS reduction ≥1, urinary IL-8 and VEGF increased, in patients without VAS reduction IL6 increased after PRP injection. Significant change of IL and VEGF was observed only in patients with a baseline OSS ≥18 but not in those with a baseline OSS <18. The PVR did not change after repeat PRP injections. All patients were free of urinary tract infection or difficult urination.

Interpretation of results
Intravesical PRP injection provides a therapeutic potential to change the interior environment of the bladder wall in patients with IC/BPS refractory to conventional therapy. The treatment is safe, but this preliminary study revealed that the therapeutic efficacy was limited. Several critical points might result in the limited successful results, including unstable platelet count, injection technique, and the volume injected. Nevertheless, the changes of urinary cytokines and VEGF in patients with VAS reduction deserve further investigation. Intravesical PRP might improve inflammation and facilitate tissue regeneration in IC/BPS.

Concluding message
The results of this study demonstrates that intravesical injections of PRP is safe and effective to increase bladder capacity and provide greater pain relief in patients with IC/PBS. The clinical effect of PRP on IC/PBS is further reflected by the changes of the urinary VEGF and cytokines levels.

Table 1. The changes of symptom scores and urodynamic parameters after PRP

	1st -PRP (BL, n=17)	2nd –PRP (n=15)	3rd –PRP (n=13)	4th –PRP (n=13)	4th –PRP-1M (n=7)
ICSI	9.7±4.2	8.3±2.8	6.8±3.5*	7.8±2.5	8.3±4.7
ICPI	9.7±3.6	8.5±3.7	8.3±3.9	8.4±3.5	7.6±5.4
OSS	19.3±7.2	16.8±6.2	15.2±6.8*	16.2±5.4	16.3±10.4
VAS	3.7±1.8	2.8±1.6*	2.1±2.1	2.0±1.6*	3.43±3.4
Frequency	14.2±9.2	12.7±6.4	10.5±3.1	10.5±3.8	9.6±3.3
FBC (ml)	199±126	255±157	313±135*	340±176*	244±151*
Qmax (ml/s)	10.5±6.8	10.0±5.8	8.7±2.7	15.6±8.6	_
Volume (ml)	208±70.8	263±95.4	249±107	318±113	_
PVR (ml)	81.7±115	104±138	98.6±94.4	48.5±43.9	_
CBC (ml)	300±158	330±98.7	348±115	368±93.7*	_
MBC (ml)	741±144	800±182	717±250	780±162	_
Glomerulation	1.4±0.6	1.3±0.6	1.3±0.6	1.3±0.5	_
GRA (0-3)	0	1.1±0.8*	1.8±0.6*	1.6±0.9*	2.0±0.8*
Platelet count	49.5±20.2	64.7±28.8*	69.1±16.5*	75.2±28.2*	

*P<0.05 compared with the baseline (1st –PRP), BL: baseline

Table 2. The changes of urinary cytokines after PRP treatment

	Baseline (n=13)	***2nd PRP (n=13)***	
IL2	1.59 ± 0.14	1.78 ± 0.30	0.028
IL6	2.16 ± 1.10	2.93 ± 2.22	0.055
IL8	17.3 ± 24.3	48.3 ± 76.9	0.019
VEGF	51.0 ± 12.0	56.5 ± 9.80	0.075

Table 3. The changes of urinary cytokines according to the baseline OSS and changes of VAS after PRP

		Baseline OSS ≥18 (n=8)	***Baseline OSS <18 (n=5)***	***P***	***VAS no reduced(n=8)***	***VAS ≥1 reduced(n=5)***	***P***
IL2	BL	1.61±0.14	1.56±0.15	0.199	1.63±0.16	1.53±0.08	0.306
	1M	1.91±0.26*	1.59±0.26		1.75±0.32	1.85±0.29	
IL6	BL	2.32±1.36	1.91±0.54	0.668	2.32±1.32	1.90±0.66	0.079
	1M	3.46±2.70*	2.10±0.81		3.55±2.71*	1.94±0.19	
IL8	BL	20.1±31.2	12.7±5.34	0.475	22.7±30.4	8.67±3.29	0.661
	1M	57.0±94.9*	34.5±39.7		56.9±95.2	34.7±38.5*	
VEGF	BL	52.1±9.21	49.3±16.6	0.391	53.6±13.5	46.9±8.78	0.188
	1M	60.6±8.56*	49.9±8.50		54.5±10.4	59.7±8.77*	

*P <0.05 compared with baseline

Disclosures

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