International United Academy of Sciences

Scientific achievements of the third millennium

Collection of scientific papers

on materials
XV International Scientific Conference

15.09.2021 г.

LJOURNAL.RU

San Francisco 2021

состояния урогенитального тракта последнего. Это позволит правильно оценить ситуацию, подобрать адекватную терапию и добиться наибольших положительных результатов в лечении.

***

1. Балабанов Д.Н. Антигенемия при урогенитальных микоплазменных инфекциях: авто-реф. дис. канд. мед. наук. Москва, 2009. 23 с.
2. Бухарин О.В., Валышев А.В., Гильмутдинова Ф.Г., Гриценко В.А. и др. Экология микроорганизмов человека. Екатеринбург: УрО РАН, 2006. 490 с.
3. Petrova M.I., Broek M., Balzarini J. et al. Vaginal microbiota and its role in HIV transmission and infection FEMS. Microbiol Rev. 2013. 37 (5): 762-792.
4. Гриценко В.А., Иванов Ю.Б. Роль персистентных свойств микроорганизмов в патогенезе эндогенных бактериальных инфекций. Вестник Уральской медицинской академической науки. 2009. 2: 35-39.
5. Ochiel D.O., Fahey J.V., Ghosh M. et al. Innate immunity in the female reproductive tract: role of sex hormones in regulating uterine epithelial cell protection against pathogens. Curr. Womens Health Rev. 2008. 4 (2): 102-117.
6. Krohn M.A., HiUier S.L., Eschenbach D.A. Comparison of methods for diagnosing bacterial vaginosis among pregnant women. J. Clin. Microbiol. 1989. 7: 1266-1271.
7. Brabin L. Interactions of the female hormonal environment, susceptibility to viral infections, and disease progression. AIDS Patient Care STDS. 2002. 16 (5): 211-221.
8. Bezirtzoglou E., Voidarou Ch., Papadaki A. et al. Hormone therapy alters the composition of the vaginal microflora in ovariectomized rats. Microb Ecol., 2008. 55 (4): 751-759.
9. Шендеров Б.А. Медицинская микробная экология и функциональное питание. Т. I. Микрофлора человека и животных и ее функции. М.: Грантъ, 1998. 288 с.
10. Коршунов Н.М., Володин Н.Н., Ефимов Б.А. и др. Микроэкология влагалища. Коррекция микрофлоры при вагинальных дисбактериозах. М.: ВУНМЦ МЗ РФ, 1999. 80 с.
11. Рищук С.В. Половые инфекции как основная причина ухудшения репродуктивного здоровья семейных пар. ТБЯЯА МЕБ1СА. 2013. 3: 5-11.

Gasparov A.S., Dubinskaya E.D., Dmitrieva N.V., Kolesnikova S.N., Holban I.V.
The effectiveness of the new intraovarial autoplasmotherapy technology in patients with low ovarian reserve

RUDN University
(Russia, Moscow)

doi: 10.18411/scienceconf-09-2021-03

Abstract

In this study, the authors presented the results of intraovarial autoplasmotherapy (PRP – platelet rich plasma) in 80 patients suffering from low ovarian reserve, “poor response” in IVF programs and ineffective IVF attempts in the anamnesis. The 1st group included 40 women who underwent intraovarial PRP by means of using stop-point navigation technology; the 2nd group included 40 women who received PRP without using stop-point navigation technology. The obtained data convincingly demonstrate that PRP with the use of stop-point navigation technology has a better effect on the ovarian function activation (an increase in anti-muller hormone (AMH), an increase in the number of antral follicles (CAF), an increase in estradiol, a decrease in follicle-stimulating hormone (FSH)), compared with PRP without the use of stop-point navigation technology.

Keywords: intraovarial autoplasmotherapy, low ovarian reserve, “poor response” in IVF programs.

Аннотация

В данном исследовании представлены результаты интраовариальной аутоплазмотерапии (PRP – platelet rich plasma) у 80 пациенток с низким овариальным резервом и «бедным ответом» в программах ЭКО и с неэффективными попытками ЭКО в анамнезе. В 1 группу было включено 40 женщин, которым проводилась интраовариальная PRP с использованием навигационной технологии стоп-точек, во 2

группу - 40 женщин, которым применяли PRP без использования навигационной технологии стоп-точек. Полученные данные убедительно демонстрируют, что PRP с использованием навигационной технологии стоп-точек лучше влияет на активацию функции яичников (увеличение антимюллерова гормона (АМГ), увеличение количества антральных фолликулов (КАФ), увеличение эстрадиола, снижение фолликулостимулирующего гормона (ФСГ)), по сравнению с PRP без использования навигационной технологии стоп-точек.

Ключевые слова: интраовариальная аутоплазмотерапия, низкий овариальный резерв, «бедный ответ» в программах ЭКО.

Introduction.

The autoplasmotherapy variants have been known and used for several centuries. The PRP (platelet rich plasma) is a concept arisen in medicine about 30 years ago which involves the use of autoplasm with the platelet content being at least 1 million in microliter (normally the platelet content is 200 thousand in microliter) [1, 2].

Platelets play an important role not only in the hemostasis process, but also induce mitogenesis, angiogenesis, chemotaxis, cell and vascular remodeling [3, 4].

The hypothesis that the growth factors stimulating cell growth contained in platelet-rich plasma can also stimulate the appearance of tumor cells has turned out to be completely untenable. Platelet growth factors are not mutagens. Natural autologous human polypeptides affect only the cell wall, but not the nucleus. Growth factor mediators cause normal gene expression, as opposed to pathological, which contributes to the appearance of a tumor [5, 6].

The use of this technology to increase the growth rate of bone structures and soft tissues was a discovery in traumatology, dentistry and surgery [7, 8, 9]. Therefore, the new technique found application in other fields of medicine – cosmetology, dermatology and gynecology [6, 10, 11].

Regenerative medicine is a very important and promising area of modern medicine. Regenerative medicine is a scientifically based technology of controlled tissue regeneration, preservation and restoration of their structures and functions [2, 6, 12].

The restoration and preservation of women and men reproductive function is an important medical and social task of modern science and clinical practice.

The aim of the study was to compare the effectiveness of various technologies of intraovarial autoplasmotherapy (PRP) with a reduced ovarian reserve.

Materials and methods.

The current prospective single-center cohort study included 80 patients with low ovarian reserve and “poor response” in IVF programs, aged thirty-five (35) years or less, AM index was less than 1.2 ng/ml and AFC was less than 5.

The AFC was calculated on the 3rd day of the menstrual cycle (MC) by means of a transvaginal sensor-using. Hormonal examination was performed on the 2-3 day of MC (anti-Mullerian hormone, follicle-stimulating hormone, Estradiol). The above-mentioned parameters were monitored before and 3 months after intraovarial plasma therapy.

Eighty (80) patients were divided into 2 groups by the random numbers method: the 1st group (40 women) – PRP with using stop-point navigation technology, the 2nd group (40 women)-PRP without using stop-point navigation technology.

The stages of intraovarial autoplasmotherapy with using stop-point navigation technology were as follows:

1. According to the patented technology, the navigation track and stop-points for the autoplasm introduction are pre-determined;
2. By means of using a single-light needle 20/21G, autoplasm is injected transvaginally, through the posterior vagina arch into the avascular central part of the ovarian medulla, at certain 4 stop-points (0.25 ml each). This is

done through a special nozzle on the sensor, taking into account the personalized navigation track formulated by 3D-ultrasound.

The above-mentioned author's technology allows to optimize a number of important factors:

1. Increased efficiency – the autoplasm introduction into a relatively large vessel reduces its effectiveness;
2. Increased efficiency – fractional injection into 4 stop-points creates several activation zones and allows to evenly distribute the autoplasm in the ovarian medulla;
3. Reduced efficiency and increased safety – vascular injury during manipulation may lead to significant or minor bleeding. Even minimal bleeding reduces the effectiveness.

The preparation of platelet-rich autoplasm was carried out according to a standard protocol [2, 3].

All the patients were informed in detail about the upcoming procedure and gave their written informed consent.

Statistical results processing was performed by means of using the IBM SPSS Statistical 21.0.0.0 and Statistica 10.0 programs optimized for Windows. The reliability of the differences in the results obtained was determined by means of using a paired or unpaired Student t-test. The differences between the groups were considered significant at $p<0.05$.

Results and Discussion.

Patients with a low ovarian reserve and "poor response" in IVF programs are an unpromising contingent of patients in terms of preserving and restoring reproductive function [13, 14].

Technologies that could help this group of patients are very much in demand by medical science and clinical practice. The use of intraovarial autoplasmotherapy (PRP) is an innovative technology in the treatment of the above group of patients. There are isolated works devoted to this problem in the available literature [15, 16].

At this stage, it is very important to show if:

1) there is a positive effect of ovarian activation from intraovarial autoplasmotherapy;
2) it is a result according to a comparison of various technological aspects of intraovarial autoplasmotherapy in patients with reduced ovarian reserve.

The results of the clinical examination and the anamnesis data did not reveal any differences between the examined groups ($p>0,05$) in such parameters as: age, body mass index (BMI), duration of infertility, frequency of primary and secondary infertility, the average number of previous IVF attempts (Table 1).

Table 1

Clinical and laboratory parameters of the 1st and 2nd patients' groups

Parameters study	*Patients of the 1st group n-40 (100%)*	*Patients of the 2nd group n-40 (100%)*
Age	*30.5 ± 1.2*	*32.9 ± 1.2*
BMI (kg/m²)	*23.4 ± 3.9*	*23.0 ± 3.3*
Duration of infertility	*3.9 ± 1.1*	*4.1 ± 1.1*
Primary infertility	*28 (70%)*	*27 (67.5%)*
Secondary infertility	*12 (30%)*	*13 (32.5%)*
Average number of previous unsuccessful IVF attempts	*2.26 ± 0.7*	*2.3 ± 0.7*
Anti-Mullerian hormone (ng/ml)	*0.41 ± 0.1*	*0.42 ± 0.1*
Follicle-stimulating hormone (IU/mL)	*21.1 ± 3.1*	*21.9 ± 3.2*
Estradiol (pg/ml)	*50.2 ± 9.3*	*52.0 ± 9.4*
AFC (Ultrasound)	*3.1 ± 0.9*	*3.2 ± 0.9*

Note – there were no significant differences between the groups (p>0.05)

Examination of ovarian reserve-markers (anti-Mullerian hormone, follicle-stimulating hormone, estradiol, AFC) convincingly demonstrated the following results:

1. An ovarian reserve-decrease in all the patients;
2. No differences between the examined groups ($p>0.05$) (Table 1).

Thus, there is only one difference between the examined groups, which is associated with the intraovarial autoplasmotherapy technology.

Table 2

Clinical and laboratory parameters before and 3 months after intraovarial autoplasmotherapy (PRP)

Parameter	The 1st group n-40 (100%)		The 2nd group n-40 (100%)		P
	Before PRP	3 months after PRP	Before PRP	3 months after PRP	
	1	2	3	4	
Anti-Mullerian hormone (ng/ml)	0.41 ± 0.1	1.1 ± 0.2	0.42 ± 0.1	0.7 ± 0.2	$P_{1-2} < 0.05$ $P_{3-4} < 0.05$ $P_{2-4} < 0.05$
Follicle-stimulating hormone (IU/mL)	21.1 ± 3.1	10.1 ± 2.2	21.9 ± 3.2	15.2 ± 2.1	$P_{1-2} < 0.05$ $P_{3-4} < 0.05$ $P_{2-4} < 0.05$
Estradiol (pg/ml)	50.2 ± 9.3	94.9 ± 5.0	52.0 ± 9.4	69.1 ± 4.7	$P_{1-2} < 0.05$ $P_{3-4} < 0.05$ $P_{2-4} < 0.05$
AFC (Ultrasound)	3.1 ± 0.9	6.9 ± 0.8	3.2 ± 0.9	4.7 ± 0.1	$P_{1-2} < 0.05$ $P_{3-4} < 0.05$ $P_{2-4} < 0.05$

Therefore, three (3) months after the intraovarial autoplasmotherapy in patients with reduced ovarian reserve, the activation of ovarian function and significant improvement of ovarian reserve indicators were observed: an increase in anti-Mullerian hormone, a decrease in follicle-stimulating hormone, an increase in estradiol and AFC (table 2).

The above-mentioned changes occur both in the 1st and in the 2nd groups, regardless of the technological aspects of the intraovarial autoplasmotherapy (Table 2).

However, it is very important from a scientific and clinical point of view to compare the results of the ovarian function activation depending on the technological treatment aspects.

Three (3) months after intraovarial autoplasmotherapy, a significant increase in anti-Mullerian hormone, a decrease in follicle-stimulating hormone, an increase in estradiol and AFC by 50-70% could be determined in patients of the 1st group compared to the patients of the 2nd group (Table 2).

Thus, the author's technique of intraovarial autoplasmotherapy by means of using the stop-point navigation technology can significantly improve the ovaries activation.

The above-mentioned results are pilot, but quite encouraging.

It is necessary to continue the research and expand its scope: to investigate the long-term results, to preserve and restore the reproductive function in the above-mentioned groups, as well as to examine other groups of patients.

Thus, the conducted study and the preliminary results obtained with an assessment after 3 months allowed the authors to form the following conclusions:

1. Intravoarital plasma therapy (PRP – platelet-rich plasma) is a method that activates the ovarian function in patients with low ovarian reserve and "poor response" in the IVF program for such markers as: increased anti-Mullerian hormone, decreased follicle-stimulating hormone, increased estradiol and AFC;

2. The author's technology of intravoarial autoplasmotherapy by means of using stop-point navigation technology (the 1st group of women) can significantly improve (on average by 50-75%) the ovaries activation by such markers as: an increase in anti-Mullerian hormone, a decrease in follicle-stimulating hormone, an increase in estradiol and AFC compared with the use of intravoarial autoplasmotherapy without stop-point navigation technology (the 2nd group of women).

***

1. Alves R., Grimalt, R. A review of platelet-rich plasma: History, biology, mechanism of action, and classification // Skin Appendage Disord. – 2018.¬ – №4. – P.18–24.
2. Marques L.F., Stessuk, T., Camargo I.C.C., Sabeh Junior, N., dos Santos L., Ribeiro-Paes J.T. Platelet-rich plasma (PRP): Methodological aspects and clinical applications // Platelets. – 2015. – № 26. – P.101–113.
3. Mazurov, A.V. (2011). Physiology and pathology of platelets. Moscow: Literra.
4. Gawaz M., Langer H., May A. Platelets in inflam-mation and atherogenesis // J. Clin. Invest. –2005. – Vol. 115. – №12. – P. 3378–84.
5. Okada M., Sagawa T., Tominaga A. Two mechanisms for platelet-mediated killing of tumour cells: one cyclooxygenase dependent and the other nitric oxide dependent // Immunology. – 1996. – Vol. 89. – № 1. – P.158–164.
6. Andia I., Abate M. Platelet-rich plasma: underlying biology and clinical correlates // Regenerative Medicine. – 2013. – Vol. 8 (5). – P. 645–58.
7. Massberg S., Konrad I., Schurzinger K. et al. Platelets secrete stromal cell-derived factor 1alphaand recruit bone marrow-derived progenitor cells to arterial thrombi in vivo // J. Exp. Med.–2006.–Vol. 203. – № 5. – P.1221–33.
8. Akhmerov, R.R., Ovechkina, M.V., Tsyplakov, D.E., Vorobyev, A.A., & Mansurova, T.G. (2013). Plasmolifting technology-as an injectable form of platelet autoplasm for the treatment of chronic periodontitis of I-II severity. Periodontics, 1(66), 45-47.
9. Sclafani A. Safety, efficacy and utility of platelet-rich fibrin matrix in facial plastic surgery // Arch Facial Plast Surg. – 2011. – Vol.13 (4). – P. 247–50.
10. Prosyannikova, N.V., Lipova, E.V., Pokrovsky, K.A., & Tarasenko, G.N. (2013). Platelet mass in chronic ulcerative skin defects. Russian Journal of Skin and Venereal Diseases, 2, 20.
11. Chang Y., Li J., Chen Y., Wei L.; Yang X., Shi Y., Liang, X. Autologous platelet-rich plasma promotes endometrial growth and improves pregnancy outcome during in vitro fertilization // Int. J. Clin. Exp. Med. – 2015. – №8. – P.1286.
12. Smith S.K. Angiogenesis and reproduction // BJOG. – 2001. – Vol. 108(8). – P.777-83.
13. Melo P, Navarro C, Jones C, Coward K, Coleman L. The use of autologous platelet-rich plasma (PRP) versus no intervention in women with low ovarian reserve undergoing fertility treatment: a non-randomized interventional study // J Assist Reprod Genet. – 2020. – Vol. 37(4). – P. 855-63.
14. Sfakianoudis K, Simopoulou M, Nitsos N, Rapani A, Pantou A, Vaxevanoglou T, Kokkali G, Koutsilieris M, Pantos K. A Case Series on Platelet-Rich Plasma Revolutionary Management of Poor Responder Patients // Gynecol. Obstet. Invest. – 2019. – Vol. 84(1). – P. 99-106.
15. Sills E.S., Rickers N.S., Li X., Palermo G.D. First data on in vitro fertilization and blastocyst formation after intraovarian injection of calcium gluconate-activated autologous platelet rich plasma // Gynecol. Endocrinol. – 2018. – № 34. – P. 756–60.
16. Farimani M., Heshmati S., Poorolajal J., Bahmanzadeh M. A report on three live births in women with poor ovarian response following intra-ovarian injection of platelet-rich plasma (PRP) //Mol. Biol. Rep. – 2019. – № 46. – P.1611–16.

Scientific publication

Scientific achievements of the third millennium

The collection of scientific papers
of the materials XV International scientific conference
"Scientific achievements of the third millennium"

Signed print 08.09.2021. Circulation 400 copies.
Format.60x84 1/16.
Paper, offset. Printing operative.
Printed by SIC "LJournal"
Editor Chief: Ivanov Vladislav