

CLINICAL EVALUATION OF INTRAUTERINE INJECTION OF AUTOLOGOUS PBMC PRIOR TO EMBRYO TRANSFER IN ivf: WE OBSERVED 30% INCREASE OF PREGNANCY RATE IN COHORT OF 133 PATIENTS OVER 38 /h4

A. Feskov¹, I. Zhylkova^{1,2}, S. Zhilkov³

¹IVF Department, Center of Human Reproduction "Sana-Med", Ukraine

²School of Medicine, Karazin Kharkiv National University, Ukraine

³R&D Department, PROGENA Inc., USA

OBJECTIVE: It is known that many older IVF patients are suffering of repeated implantation failure (RIF) and peripheral blood mononuclear cells (PBMC) can treat RIF. We hypothesize that the age-related risk of implantation failure may be overlapping, in etiology, with RIF's one. Assuming so, we evaluate clinical usefulness of intrauterine injection of PBMC applied for all aged IVF patients (RIF & non-RIF).

DESIGN: Non-randomized controlled study in single IVF center with in-house laboratory for manufacturing of PBMC product

MATERIALS AND METHODS: During 2012-2014 in our center, we proposed PBMC product (at subsidized price) to all IVF female patients of age 38-45 with normal uterine cavity, who had at least two top quality embryos (non-donated) for transfer. Number of previous IVF attempts was not counted in attention. Exclusion criteria were: any serious systemic disease or endocrine disorders; other criteria. Patients, who agreed to take the PBMC, formed a 1st group (G1, N=94) and proceeded to the treatment under IRB approval; those who declined were the control (G2, n =39); total 133 cases in two-group cohort. The subgroups were: 49 patients of age 38-40 in G1 vs 24 in G2; 26 of 41-42 in G1 vs 12 in G2; 19 of 43-45 in G1 vs 3 in G2. Composition of PBMC with human chorionic gonadotropin (HCG) was produced according to the process disclosed in US patent 20130172666. Prior to embryo transfer (ET), the composition was delivered through catheter as intrauterine injection in amount 0.15 mL of a suspense containing certain concentrations of HCG and PBMC per dose. ET of two top quality embryos was performed 24 to 72 hours following the injection. Three weeks after said ET, the standard ultrasound diagnostics was applied to determine a clinical pregnancy. Chi-squared test was used for statistical analysis of results.

RESULTS: Clinical pregnancy rate in PBMC group (26.6%) was 30% higher, than in control group (20.5%). 25/94 patients became pregnant in G1 vs 8/39 patients in G2 (p=0.46). Observations were rather favorable for use of PBMC, especially assuming that oldest subgroup 43-45 was disproportionally larger in the PBMC group, than in control (19/94 vs 3/39). Among oldest patients, there were 4/19 pregnancies with PBMC use and 0/3 without it (p=0.38). Larger cohort is needed for statistical significance of observations.

CONCLUSIONS: For the first time we demonstrate clinical usefulness of autologous PBMC therapy for aged IVF patients. Our observations are highly suggestive in support of intrauterine use of PBMC+HCG for females over 38; it may lead to early signaling of immune cells to mother's body on systemic level and early preparation of endometrium environment on local level prior to ET. Age-related risk of implantation failure is reduced: we see better inducing of pregnancy in case of PBMC-enhanced IVF treatment, compared to conventional one. We initiate multi-center study for statistically significant verification of upgraded IVF protocol.

SUPPORT: Progena Inc. provided intellectual property and financing for manufacturing of PBMC product in in-house laboratory of Center of Human Reproduction "Sana-Med"; product was subsequently used in IVF Department there.

Group\\ Sub-group	Age 38-40	Age 41-42	Age 43-45	Total	Preg.	Preg. Rate
PBMC (Preg.%)	49 (30.6%)	26 (23.1%)	19 (21.1%)	94	25	25/94= 26.6%
Control (Preg.%)	24 (25.0%)	12 (16.7%)	3 (0.0%)	39	8	8/39= 20.5%