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G-CSF Mobilized Plasma Regenerate Ovarian Stroma and Restore Ovarian Function.

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Abstract:

Introduction: Tissue regeneration has been achieved in aged mice by young blood administration. Moreover, optimization of ovarian reserve biomarkers has been correlated with the presence of stem cell secreted factors in plasma from poor responder women (PR), undergoing autologous stem cell ovarian transplant, after granulocyte colony stimulating factor (G-CSF) mobilization. Thus, we aimed to analyze if G-CSF mobilized plasma could induce fertility rescue in mouse models of ovarian damage.

Methods: Diminished ovarian reserve (DOR) and premature ovarian insufficiency (POI) were induced in NOD/SCID mice using 12 mg/Kg cyclophosphamide (Cy) + 1,2 mg/kg busulphan (Bu) or 120 mg/Kg Cy + 1,2 mg/kg Bu, respectively. One week later, mice received intravenous injections of: peripheral blood plasma (Control group, n=11) or G-CSF mobilized plasma (G-CSF group, n=11) from PR. Plasma was administered every other day during 2 weeks. Then, 7 mice/group were sacrificed to analyze ovarian stroma while the remaining ones underwent consecutive mating to assess the long-term reproductive outcomes. Wild-type mice were used for reference values (w/o chemotherapy and w/o plasma).

Results: G-CSF plasma increased microvessel density (DOR: Control 8.5±1.3% vs. G-CSF 13.5±3.9%, p=0.03 and POI: Control 4.3±1.2% vs. G-CSF 16.8±0.3%, p=0.01) recovering wild-type reference levels for ovarian vascularization (12.8±0.0%). In addition, G-CSF plasma improved cell proliferation (DOR: Control 0.2±0.0% vs. G-CSF 4.0±0.6%, p<0.01; POI: Control 0.1±0.0% vs. G-CSF: 0.6±0.4%, p=0.05) while decreased expression of the apoptotic protein cleaved-caspase 3 in the DOR model (DOR: Control 1.4±0.2 vs. G-CSF 0.4±0.1; p<0.01). Regarding long-term fertility potential, G-CSF plasma increased pregnancy rate in the POI model, where controls were not able to achieve any spontaneous pregnancy (POI: Control 0% vs. G-CSF: 40%), and allowed the birth of healthy pups (POI: Control 0±0 vs. G-CSF 7±1). These positive effects were also observed in the DOR model, although differences were not statistically significant (pregnancy rate: Control 36% vs. G-CSF 42%; litter size: Control 7±1 vs. G-CSF 8±1).

Conclusion: G-CSF plasma promoted ovarian function recovery by regenerating the ovarian stroma vascularization and proliferation, allowing spontaneous pregnancies and birth of healthy pups. Funded by the PROMETEO/2018/137 grant - Valencian Regional Government

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Category (Complete): 11.8 - Basic Reproductive Biology: Regenerative Medicine
Presentation Preference (Complete): Either Oral or Poster
Questionnaire (Complete):
Has this abstract been previously presented as it is written?: No
Has this abstract been partially presented?: No
My submitted abstract(s) contains original data, written in standard scientific form, complete with numeric values and statistical analyses when appropriate.: Yes
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Translational Value: Yes
Please describe the translational relevance below : G-CSF plasma could be a therapeutic alternative, non-invasive and from autologous origin, for patients with impaired ovarian reserve

Keyword (Complete): Ovarian rejuvenation ; Fertility rescue ; G-CSF mobilized plasma
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