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Application of cryopreserved umbilical cord blood and placenta-derived products in the treatment of infertility in a patient with diminished ovarian reserve. Case report

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Diminished ovarian reserve (DOR) is a condition characterized by reduction of the oocyte quantity and quality. The causes: advanced age, genetic predispositions, autoimmune diseases, iatrogenic causes, lifestyle-related factors. Diagnosis relies on ovarian reserve markers: anti-Müllerian hormone (AMH) and antral follicle count (AFC). Many DOR women can't conceive naturally, they undergo assisted reproductive technologies (ART), but it often shows limited success. Traditional treatment includes hormone therapy, ovulation stimulation, but effect is limited in the use of the available follicular pool. Regenerative approach involving cryopreserved umbilical cord blood (CUCB) and placental-derived products (PDP) are being studied. Treatment with cryopreserved preparations is a part of Clinical Trials "Investigation of the possibility and effectiveness of the use of CUCB stem cells and PDP for the correction of reproductive function disorders of psychosomatic origin in women and men" No. 0119U100443.

This case report shows use of cryopreserved cord blood and placental-derived preparations in an iatrogenic DOR. A 37 y.o. woman appealed to Clinic of professor Feskov with a 6-year history of primary infertility. She had hypothyroidism and got relevant endocrinological care. She underwent 3 laparoscopies: dermoid cyst removal on the right and follicular cyst excision on the left (2015); apoplexy of the left ovary followed with partial resection (2017); adhesiolysis and tube passage test (2020). Anti-Müllerian hormone (AMH) level was critically low — 0.2 ng/mL FSH — 27.09 mIU/mL, LH — 61.17 mIU/mL, estradiol — 39.51 ph/mL. Her partner's sperm was fertile: concentration 57 million/mL, progressive motility 40, 19% normal morphology. She had 2 unsuccessful IVF in another clinic. In our clinic, a third IVF cycle was conducted with preimplantation genetic testing (PGT-A), the dose of FSH was 300IU: 2 oocytes retrieved. One embryo was biopsied and resulted aneuploid. According to the woman's history of surgical intervention, DOR, failed IVF attempts, we proceeded to stem-cell therapy. The therapeutic regimen was intramuscular applications of cryopreserved cord blood suspension injected twice over two weeks and subcutaneous application of a cryopreserved placental fragment. The next IVF cycle: 5 oocytes retrieved, 4 MII were fertilized using ICSI. 2 blastocysts were biopsied on 5th day, 1 was an euploid. The embryo transfer was in a frozen-thawed cycle, in 3 weeks a clinical pregnancy was diagnosed. The course of pregnancy was physiological, at 40 weeks' gestation, a healthy baby was born via vaginal delivery. Baby's cord blood and placenta were cryopreserved in clinic's cryobank. The patient, previously unresponsive to many ARTs showed improved response in. While a positive outcome cannot reflect general therapeutic efficacy — it underlines the need for well-designed controlled studies and careful patient selection.

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Biochemical markers of cholestasis in rats with acetaminophen-induced intoxication after partial hepatectomy

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Currently, partial liver resection is widely used in surgical practice for hepatobiliary tumors, toxic injuries, as well as in transplantation (Sun, 2021). This becomes possible due to the liver's ability to regenerate in response to tissue loss with the restoration of the hepatostat and the functional potential of the organ. At the same time, impairment of hepatoregeneration processes acts as a predictor of liver failure, which often develops against the background of cytolytic and cholestatic syndromes (Rodimova, 2023; Bhushan, 2023). The aim of the study was to assess the dynamics of biochemical markers of cholestasis in the blood serum of rats with acetaminophen-induced toxic injury following partial hepatectomy.

White non-linear rats were divided into two groups: (1) control animals with resection of 2/3 of the liver (C/PH), and (2) rats with acute acetaminophen-induced injury, which underwent partial hepatectomy (TI/PH). Biochemical tests on alkaline phosphatase (ALP) activity, total bilirubin (Bili-T) level and its fractions were conducted at 0 (preoperative phase), 24, 48, 72, and 168 hours after hepatectomy. In the blood serum of control rats after PH, an increase in ALP activity was revealed during the 72 h of the regeneration process (24 h — 42%; 48 h — 47%; 72 h — 36%) compared to the preoperative level. The total bilirubin content in animals of the C/PH group exceeded preoperative values by 61—65% during the 48 h of the regeneration period, with the increased levels of direct bilirubin by 63—67% and indirect bilirubin by 58—63%. Meanwhile, in animals of the TI/PH group, an increase in serum ALP activity and total bilirubin levels was recorded throughout the entire experiment (168 h), mainly due to the indirect bilirubin fraction, with a maximum at 72 h (ALP: 66%; indirect bilirubin: 90%) relative to preoperative values in rats of the toxic injury group. The increase in serum ALP levels is probably associated with the intensification of enzyme synthesis due to cholangiocyte proliferation following a 2/3 liver resection. At the same time, hyperbilirubinemia may be caused by impaired bilirubin uptake and insufficient glucuronidation due to the increased demand for the conversion of high doses of acetaminophen under significant functional load on the remaining part of the liver after PH. ALP hyperenzymemia and hyperbilirubinemia during the 7 days of the experiment in animals of the TI/PH group are likely to indicate the formation of signs of functional insufficiency of liver cells already in the preoperative term, with a simultaneous decrease in their number under the studied conditions. Thus, liver regeneration in rats with toxic injury after partial hepatectomy is accompanied by an increase in cholestasis markers (ALP and Bili-T, mainly due to its indirect fraction) during the 7-day experimental term. The obtained results may be useful for assessing the functional state of the liver in the postsurgery period against the background of drug-induced toxic lesions, especially in clinical situations that require the transplantation of cryopreserved hepatocytes as one of the approaches to liver recovery.