FIBRIN-BASED BIOMATERIAL FOR OVARIAN TISSUE ENCAPSULATION AND CRYOPRESERVATION AS ALTERNATIVE APPROACH FOR FERTILITY PRESERVATION IN CANCER PATIENTS

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Abstract Body

This study aimed to investigate effects of fibrin-based hydrogel encapsulation with or without VEGF (vascular endothelial growth factor) on follicle quality and cell survival signaling pathway after ovarian tissue cryopreservation. Ovarian cortex was obtained from 7 women (age 44-47 years old) with surgically indicated benign diseases. Each was sub-divided into four groups; I) fresh control, II) ovarian tissue cryopreservation without encapsulation, III) fibrin (10 mg/mL fibrinogen plus 50 IU/mL thrombin) encapsulated tissue without VEGF and IV) encapsulated tissue with 0.1 ng/mL VEGF. All designed experimental cohorts were cryopreserved by slow freezing. Outcome assessment included follicle viability, cell survival and metabolism signaling pathway (Bcl-2, Caspase-3 and 9, ATP-6 gene and ERK-1/2 protein expression levels). Our results revealed that percentages of follicle viability and normal morphology without pyknosis or nuclear fragmentation and granulosa cell disruption were significantly decreased after freezing procedure. Greater percentage of follicle viability was observed in encapsulated tissue with or without VEGF compared to non-encapsulated group (78.8 ± 5.1 vs 76.4 ± 5.9 vs 75.3 ± 7.9; mean ± S.D.). However, statistical differences among frozen-thawed groups were not remarked. Similar to histological findings, cell survival gene expression levels (Bcl-2, Caspase-3 and 9) were down-regulated after cryopreservation. Furthermore, ATP-6 did not change among non or encapsulation tissues (P = 0.836). ERK-1 protein kinase implicated in cell proliferation and differentiation present in encapsulated samples (0.35 ± 0.22 in Group III and 0.36 ± 0.22 in Group IV; mean S.D.) could maintain its activity as manifested in fresh cortical strips (0.41 ± 0.31; mean ± S.D) (P = 0.712 and 0.714, respectively). In conclusion, our data preliminarily proposed applicable biomaterial technology to create optimal intra-ovarian cortex environment during cryopreservation. More studies on novel tissue engineering should be further developed for beneficial results in cancer patients who prefer to preserve their fertility

Keywords: Cryopreservation, Encapsulation, Fibrin, Ovarian Tissue, Vascular Endothelial Growth Factor