NUCLEATED PERIPHERAL BLOOD CELLS RESTORE FERTILITY TO CHEMOTHERAPY-TREATED MICE

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Abstract: Generally, cancer chemotherapeutic agents contribute to infertility by destroying antral follicles. However, it is not clear whether cell-based intervention can restore fertility to chemotherapy-treated patients. The objective of this study was to determine whether nucleated peripheral blood cells (NPBC) can reverse ovarian failure (OF) induced by cancer chemotherapy (CTX). To accomplish this task, a complete randomized design was used in two experiments (EXPTs) to study OF and its reversal with NPBC in adult SV-129 female mice. Five to 6 week old SV-129 female mice were randomly assigned to 3 groups (A, B and C). In groups A & B, OF was induced with a combination of intraperitoneal injections of 12 mg busulfan/kg in DMSO and 120 mg cyclophosphamide/kg in saline (hereafter this combination will be designated as chemotherapy [CTX]). Mice in group C were similarly injected with CTX vehicles. Mice in group A received NPBC (2 x 10\textsuperscript{6} cells/mouse) from healthy SV-129 mice, while mice in groups B and C received saline, 7 days later. Half the population of mice/group was used to study the efficacy of NPBC to restore fertility indices to mice whose ovaries were induced to fail with CTX. The remaining half was immediately subjected to breeding studies to determine whether NPBC infusion contributes to improved litter size in CTX-treated mice. Estrous cycle length increased significantly in mice treated with CTX compared with untreated mice. This increase occurred at proestrus and diestrus I stages of the estrous cycle. Infusion of CTX-treated mice with NPBC reduced the estrous cycle length (P<0.05) from 18 days observed among CTX-only treated mice to 7 days. NPBC enhanced the expression of StAR protein in the follicles of CTX-treated mice, an indication of enhanced folliculogenisis which ultimately led to increased number of ovulated mature eggs and consequently, increased litter size. This study shows a successful restoration of fertility to CTX-treated mice by NPBC. We contend that NPBC potentially contain significant numbers of bone marrow derived stems cell that can migrate to the ovaries, restore folliculogenisis and hence restore fertility in CTX-treated mice.

Key words: Busulfan, cyclophosphamide, Chemotherapy, StAR protein, Estrous cycle, Litter size.

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