ANTIMETABOLITE CANCER DRUG GEMCITABINE IMPACTS PREANTRAL AND ANTRAL FOLLICLE COHORTS IN THE OVARY

O. Oktem, A. Yuksel, F. Unal, Y. Guzel, M. Polat, S. Aksoy, B. Urman
Obstetrics and Gynecology, Koc University School of Medicine, Turkey

Objective: Gemcitabine is a pyrimidine analog chemotherapy drug mainly used in the treatment of non-small cell lung cancer, and the cancers of pancreas, bladder and breast. Since there is no data in the literature regarding its ovarian toxicity, we aimed to determine the gonadotoxic potential of this drug in the ovary.

Materials and Methods: Fifty-four 4-6 week old Sprague-Dawley young female rats were either given saline injections only (control) or single dose of gemcitabine at 100 and 200mg/kg intraperitoneally. Each group has 18 animals. The animals were euthanized 72 hrs later. Healthy and atretic follicle fractions of primordial, primary, preantral and antral follicles were determined. Antimullerian hormone (AMH) levels were measured. Follicle counts were expressed as the mean number of follicles per mm².

Results: Healthy and atretic fractions of primordial and primary follicles were comparable in control animals and those treated with gemcitabine 100 and 200mg/kg. However, the numbers of healthy preantral and antral follicles were significantly lower, and the atretic preantral and antral follicles were significantly higher in the ovaries exposed to gemcitabine 100 and 200 mg/kg compared to controls (FIGs 1A-1B-1C). Accordingly, AMH levels in the animals treated with gemcitabine 100 and 200mg/kg were significantly lower compared to control animals (FIG-1D).

Conclusion: This study provides a histomorphometric and biochemical evidence that antimetabolic chemotherapy agent gemcitabine has more toxic effects on growing follicle fractions than dormant primordials, possibly due to higher metabolic demand and mitotic activity of the expanding granulosa cell layers in the preantral and antral stage follicles.

1A Healthy follicle fractions
1B Atretic follicle fractions
1C Control
1D AMH