HOW BISPHENOL A CONTRIBUTES TO OVARIAN CANCER: SHIFTS IN EPITHELIAL CELL VARIETY, CELL DEATH, AND THE BODY'S ANTIOXIDANT AND ANTI-INFLAMMATORY RESPONSES

.

Dr Mahima Sara Mathew

Assistant professor in the Department of Dermatology

Samarkand State Medical University

Abstract

This study aimed to investigate the cancer-causing effects of Bisphenol A (BPA) on ovarian epithelial cells. Over four months, mice were given low (LD, 1 mg/kg) or high (HD, 5 mg/kg body weight) doses of BPA every other day via oral gavage, while the control group received corn oil through the same method. Histopathological analysis revealed that repeated BPA exposure led to a borderline epithelial tumor, characterized by changes in epithelial structure and the formation of branching papillae. As a result, BPA exposure modifies ovarian antioxidant, apoptotic, and inflammatory gene expression, alters EC diversity, and causes mortality.

Keywords: ovarian epithelial cells, ovarian cancer, cell death, antioxidant, anti-inflammatory, bisphenol A, gene expression, epithelial tumor, endocrine-disrupting chemicals, natural hormones.

Доктор Махима Сара Мэтью

Доцент кафедры дерматологии

Самаркандский государственный

медицинский университет

Аннотация

Целью данного исследования было изучение канцерогенных эффектов бисфенола А (БФА) на эпителиальные клетки яичников. В течение четырех месяцев мышам давали низкие (LD, 1 мг/кг) или высокие (HD, 5 мг/кг массы тела) дозы БФА через день через желудочный зонд, в то время как контрольная группа получала кукурузное масло тем же методом. Гистопатологический анализ показал, что повторное воздействие БФА

привело к пограничной эпителиальной опухоли, характеризующейся изменениями в эпителиальной структуре и образованием разветвленных сосочков. В результате воздействие БФА изменяет антиоксидантную, апоптотическую и воспалительную экспрессию генов яичников, изменяет разнообразие ЕС и вызывает смертность.

Ключевые слова: эпителиальные клетки яичников, рак яичников, гибель клеток, антиоксидант, противовоспалительный, бисфенол А, экспрессия генов, эпителиальная опухоль, химикаты, нарушающие работу эндокринной системы, естественные гормоны.

Introduction

Human infertility and subfertility are caused by a class of chemicals known as endocrine-disrupting chemicals (EDCs), which interfere with the natural hormones' ability to function [1]. Natural hormones, which are essential for controlling growth, reproduction, development, and behavior, are inhibited by these exogenous substances [2]. Sterility, unbalanced sexual behavior, thyroid and adrenal cortical dysfunctions, elevated cancer risk, birth defects, immunosuppression, heightened immune responses, and autoimmunity are all consequences of exposure to EDCs [3,].

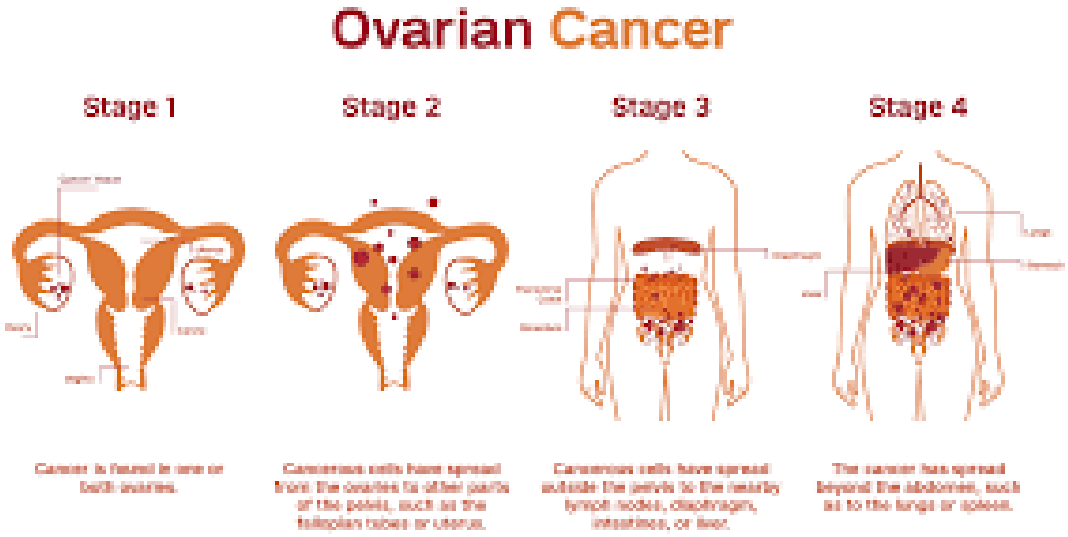
One of the most extensively researched and widely distributed EDCs is bisphenol A (BPA). Epoxy resins and polycarbonate polymers, such as polyester, polysulfone, polyacrylate, and polyetherimide, are frequently synthesized using BPA . In many Asian nations, the daily intake of BPA is estimated to be between 1.61 μg and 5.19 μg [4].

Research on BPA's toxicity to reproduction has been extensive. Reproduction and development issues result from BPA's disruption of hormones through interactions with oestrogen, androgen, and thyroxine receptors . Pregnancy-related exposure to BPA increases ovarian cysts and causes aneuploidy in maturing oocytes, while also promoting early puberty, early vaginal opening, ovarian dysfunction, and primordial follicle loss in offspring [5].

Oestrogen and progesterone, which control the reproductive cycle, are produced by the ovary in females and aid in the growth of oocytes. Most of the ovary is covered by ovarian surface epithelium (OSE). Throughout the repeated cycles of rupture and repair during ovulation, it experiences structural changes that result in the formation of inclusion cysts.

There are cuboid or simple pseudostratified epithelium in the epithelial layer. Moreover, Ly6A+ stem cells with a greater capacity for carcinogenesis are found

in the hilum region . These cells divide and repair the damaged ovarian surface during ovulation. There are two sources of OSE cells: the hilum comes directly from the mesonephros, whereas the majority of cells come from the GREL cells, which are derived from the mesonephros [6]. Additionally, the ovary is home to a variety of cell types, such as somatic cells such as endothelial cells, granulosa cells (GC), theca cells (TC), and immune cells, as well as germ cells, which are different stages of oocytes [7]. While endothelial cells remove waste and supply nutrients, immune cells (lymphocytes and macrophages) are involved in immunological response and tissue remodeling . BPA disrupts the normal development of follicles and has an impact on ovarian function . Because BPA has an oestrogenic effect, it disrupts reproductive processes by encouraging apoptosis and cell cycle inhibition of GC [8]. Through oxidative stress, ERK/AKT/NF-κB signaling, and reproductive function, BPA affects inflammatory processes and cellular proliferation in human endometrial stromal cells [9]. While a number of researchers have examined the harmful effects of BPA on ovarian cells, a thorough investigation of ovarian epithelial cells (OECs) has not yet been conducted. In general, BPA exposure causes death and changes the expression of genes that suppress tumors, inflammation, and apoptosis inside the ovary. Figure1. Stages of the ovary cancer.



Materials and methods

Mice given BPA had their ovaries examined for histopathological alterations. Normal ovaries in untreated mice have a monolayer of microscopically flat, cuboidal to pseudostratified columnar cells with varying stages of follicles and smooth surface epithelium. The ovarian tissues of BPA-treated mice displayed a disordered epithelial morphology with branching papillae, stratified epithelium with stromal core, and homogeneous nuclear characteristics, which could be a sign of low-grade

Discussion and Results

BPA is an endocrine disruptor that leads to a number of reproductive abnormalities in people. It disrupts ovarian follicle maturation and induces inflammation in females [7], [8]. We previously demonstrated that BPA causes inflammation in the uterus and ovaries and raises the production of cancer stem cells in the ovaries [9]. We examined the effects of repeated LD (1 mg/kg BW) and HD (5 mg/kg BW) BPA administration on OECs, PDPL and CD74 receptor expression, and apoptotic.

In conclusion

The ovarian epithelial surface changed after BPA treatment, exhibiting branching papillae, a sign of a borderline low-grade epithelial neoplasm. In mice treated with BPA, the diversity of ECs was altered. The administration of BPA causes ovarian cell death and alters the expression of the PDPL and CD74 receptors. Molecular alterations in BPA-treated ovaries reveal modifications in antioxidant, apoptotic, anti-inflammatory, and tumor suppressor genes.

References:

1.N. Hamid *et al.*Combined toxicity of endocrine-disrupting chemicals: a review Ecotoxicol. Environ. Saf. (2021)

2.S. Eladak *et al.*A new chapter in the bisphenol A story: bisphenol S and bisphenol F are not safe alternatives to this compound. Fertil. Steril. (2015)

3.D.D. Seachrist *et al.*A review of the carcinogenic potential of bisphenol A .Reprod. Toxicol. (2016)

4.T. Geens *et al.*Are potential sources for human exposure to bisphenol-A overlooked?

Int. J. Hyg. Environ. Health. (2011)

5.L.N. Vandenberg *et al.*Human exposure to bisphenol A (BPA).Reprod. Toxicol. (2007)

6.S. Lu *et al.*Estimation of intake and uptake of bisphenols and triclosan from personal care products by dermal contact. Sci. Total Environ.(2018)

7.T. Geens *et al.*A review of dietary and non-dietary exposure to bisphenol-AFood Chem. Toxicol.(2012)

8.G. Russo *et al.*Monitoring of bisphenol A and bisphenol S in thermal paper receipts from the Italian market and estimated transdermal human intake: a pilot study. Sci. Total Environ.(2017)

9.M. Uzumcu *et al.*Developmental exposure to environmental endocrine disruptors: consequences within the ovary and on female reproductive function.Reprod. Toxicol.(2007)