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Epub 2017 Jun 23.

Estrogen–gut microbiome axis: Physiological and clinical implications

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PMID: 28778332 DOI: 10.1016/j.maturitas.2017.06.025 

Abstract

Low levels of gonadal circulating estrogen observed in post-menopausal women can adversely impact a diverse range of physiological factors, with clinical implications for brain cognition, gut health, the female reproductive tract and other aspects of women's health. One of the principal regulators of circulating estrogens is the gut microbiome. This review aims to shed light on the role of the gut microbiota in estrogen-modulated disease. The gut microbiota regulates estrogens through secretion of β -glucuronidase, an enzyme that deconjugates estrogens into their active forms. When this process is impaired through dysbiosis of gut microbiota, characterized by lower microbial diversity, the decrease in deconjugation results in a reduction of circulating estrogens. The alteration in circulating estrogens may contribute to the development of conditions discussed herein: obesity, metabolic syndrome, cancer, endometrial hyperplasia, endometriosis, polycystic ovary syndrome, fertility, cardiovascular disease (CVD) and cognitive function. The bi-directional relationship between the metabolic profile (including estrogen levels) and gut microbiota in estrogen-driven disease will also be discussed. Promising therapeutic interventions manipulating the gut microbiome and the metabolic profile of estrogen-driven disease, such as bariatric surgery and metformin, will be detailed. Modulation of the microbiome composition subsequently impacts the metabolic profile, and vice versa, and has been shown to alleviate many of the estrogen-modulated disease states. Last, we highlight promising research interventions in the field, such as dietary therapeutics, and discuss areas that provide exciting unexplored topics of study.

Keywords: Cancer; Dysbiosis; Estrobolome; Fertility; Metabolic syndrome; Phytoestrogen.

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