STUDENTS' CORNER
LETTER TO THE EDITOR

Is Metformin effective in Breast Cancer (BC) patients without Type 2 Diabetes (T2D)?

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Dear Editor, Metformin is a biguanide antihyperglycaemic agent used as a first- choice medication for alleviation of Diabetes Mellitus type 2 (T2D). It acts by suppressing hepatic glucose production, by increasing sensitivity of tissues to insulin and by causing a marked increase in GDF15 secretion resulting in reduced hunger and calories consumption. In addition, it's also been found relevant in management of number of cancers due to its action like activation of adenosine monophosphate kinase, limiting insulin growth factors or insulin and suppression of oxygen radicals produced within the body and its subsequent harmful effects to deoxyribonucleic acid (DNA) molecule.[1] One of the said cancers is Breast cancer (BC).

Breast cancer is the most common malignancy in the globe. In 2020, it was diagnosed in 2.3 million women worldwide, with 685000 deaths globally, and 7.8 million women were living with BC history in the past five years.[2] According to World Health Organization, 25,928 people were diagnosed with breast cancer and 13,725 deaths were reported in Pakistan as of 2020.[3] Various observational and preclinical studies have shown metformin to be a potential antiproliferative agent in BC subtypes.[4] Said studies involved a patient who also had diabetes. Those findings intrigued trials of the use of metformin for patients with breast cancer without diabetes and results have been quite disappointing.

According to Ma.32 which is a randomized double blind placebo controlled phase 3 trial, among 2533 patients with hormone receptor–positive disease, the incidence of invasive disease–free survival events was 2.78 per 100 patient-years with metformin in contrast to placebo with 2.74 per 100 patient-years (hazard ratio [HR], 1.01; p=0.93). Among 1116 patients with hormone receptor–negative disease, the findings of relapse-free survival events was 3.58 with metformin contrary to placebo with 3.60 (HR, 1.01; p=0.92). However, through exploratory analysis, in a small subset of HER2- positive patient with the rs11212617 single nucleotide variant's any C allele, there were 1.93 disease-free survival events with metformin per 100 patient-years, compared to 3.05 events with placebo (HR, 0.64, p=0.03)[5] but results need to be confirmed in randomized trial as it was exploratory analysis.

Although this is yet to be tested in larger and additional trials, metformin didn't significantly improve relapse free survival of high risk surgically resectable breast cancer patients without diabetes and should be immediately stopped if being prescribed in patients of such category.

Disclaimer: None.

Conflict of interest: None.

Funding disclosure: None.

DOI: https://doi.org/10.47391/JPMA.7684

Submission completion date: 27-08-2022

Acceptance date: 28-11-2022

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