Plasma levels of markers for therapeutic advances among breast cancer patients undergoing chemotherapy

¹ Jyoti Bala Chauhan, ² Girish Chandran
¹ Professor and Head, ² Assistant Professor
¹Department of Biotechnology, Microbiology, Biochemistry and Botany
¹Pooja Bhagavat Mahajana Memorial Education Centre
PG Wing of SBRRMFGC, Metagalli, Mysuru-570016, India

Abstract: Though the breast cancer deaths have been marginally reduced globally due to the diagnostic tools/ therapies, it is crucial to investigate the relative hazardous factors and methods to improve prognosis especially during chemotherapy. For many malignancies, serum tumor markers play an important role in patient management during initial diagnosis and in the course of chemotherapy. In breast cancer, however, the role of serum markers is less well established owing to limitation in such studies. The obvious dyslipidemia and lowered total plasma cholesterol among breast cancer patients, needs to be well studied for establishing the link between the plasma lipid profile and pathophysiology of the breast cancer.

Index Terms - Breast cancer, early markers, plasma lipid profile, total plasma cholesterol,

I. INTRODUCTION

Breast cancer is the most commonly diagnosed cancer and the second leading cause of cancer-related death among women globally (Autier, et al., 2017). However, currently the female breast cancer mortality is comparatively reduced owing to the early diagnostic tools and treatment efficiency. It is still crucial to investigate the relative hazardous factors and methods to improve prognosis especially during chemotherapy (Medical Advisory Secretariat, 2010).

Diagnosis of breast cancer

Mammography is a widely used screening approach in the detecting of breast cancer and has helped monitor the disease progress and therapy effectively. The other major screening methods, such as Magnetic Resonance Imaging (MRI), sensitive than mammography are also being utilized for breast cancer diagnosis. However, early markers of the breast cancer are being reported constantly from various clinical groups which would design an early level diagnostic tool battery to assess the incidence of breast cancer.

Major risk factors of breast cancers

There are numerous risk factors such as sex, aging, estrogen, family history, gene mutations and unhealthy lifestyle, for the etiology of breast cancer (Grech et al., 2015). Although the incidence rate of breast cancer is increasing annually while the mortality rate decreases due to the widespread early screenings/ therapy. Biological therapies have been developed in recent years and proved to be beneficial for breast cancer (Soucek et al., 2018).

Types of breast cancers

The types include: Non-Invasive Breast Cancer cells; Invasive Breast Cancer cells: Ductal carcinoma in situ (DCIS): Lobular carcinoma in situ; Infiltrating lobular carcinoma (ILC):: Infiltrating ductal carcinoma (IDC); Medullary carcinoma; Mutinous carcinoma; Tubular carcinoma; Inflammatory breast cancer; Paget's disease of the nipple; and Phylloides tumor.

Serum or plasma markers for Breast Cancer

For many malignancies, serum tumor markers play an important role in patient management during initial diagnosis and in the course of chemotherapy. In breast cancer, however, the role of serum markers is less well established owing to limitation in such studies. The most widely used serum markers in breast cancer are CA 15-3 and carcinoembryonic antigen (CEA). Less widely used markers include BR 27.29, tissue polypeptide antigen (TPA), tissue polypeptide specific antigen (TPS) and the shed form of HER-2. Numerous studies suggest significant hepatotoxicity during chemotherapeutic cycles. Hence, hepatic markers in the plasma are a requisite to monitor the whole body health during chemotherapy (Lappano et al., 2018). The cancer cells are shown to extensively use glucose for proliferation. Elevated glucose metabolism toward the pentose phosphate pathways is one of the pivotal metabolic characteristics of malignant cells (Chimento et al., 2018). Additionaly, due to the mitogenic property of insulin, glucose metabolism is considered crucial for the cancer cell survival. Intraportal insulin levels influence IGF-I bioavailability. IGF-I is a small peptide (7.5kd) with significant structural homology with pro-insulin and insulin, and is regulated by growth hormone. IGF-I is involved in stimulation of multiple cellular responses that are related to growth, including synthesis of DNA, RNA, and cellular proteins.

Cholesterol is a quintessential structural ingredient of the plasma membrane. Proliferating cells, such as cancer cells, are believed to have increased requirements for cholesterol (Bathaie et al., 2017). To overcome its needs, tumor cells can increase lipid biosynthesis, but can also uptake cholesterol from the bloodstream. The efficacy of cancer cell to use exogenous lipids has indicated to explain the association between dyslipidemia and high fat diets with cancer. However, it should be noted that several of those studies did not account for the lipoprotein fractions, lipid lowering drugs use or the different tumor types, which could all influence the results and their interpretation. Therefore currently understanding about the importance of plasma cholesterol in cancer progression remains poorly established (Hashemi et al., 2017).

Complete blood count along with plasma analysis is a prerequisite investigation for breast cancer patients before the use of any treatment. Though chemotherapy destroys cancer cells, some of the normal cells are also sensitive to these treatments and get damage in the process. Some cancer treatments interfere with blood cells production of the body. Complete blood counts are routinely performed during chemotherapy and other breast cancer treatments to check the number of each type of blood cell circulating in the body.

An unbalanced lipid profile with high total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), triglycerides (TG), and low high-density lipoproteincholesterol (HDL-C), apolipoprotein A1(Apo-A1), apolipoprotein B (Apo-B) is an established risk factor of cardiovascular diseases. LDL-C has been successfully treated by lipid-lowering therapies. Plasma lipids and lipoproteins are closely associated with breast cancer risk factors which suggest the role of lipids in causing breast cancer (Likus et al., 2016). Furthermore, HDL-C level is associated with several other breast cancer risk factors. Several studies have reported the association between lipids and breast cancer. However, the results are controversial. Some prospective clinical studies reported that high levels of total cholesterol and HDL-C may increase breast cancer incidence. However, others have suggested that low total cholesterol and HDL-C levels could increase breast cancer risk. Few researches have studied the status of lipid in breast cancer patients during the course of chemotherapy.

Conflict of Interest

Authors declare that there is no conflict of interest.

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References

Autier, P., Boniol, M., Koechlin, A., Pizot, C., & Boniol, M. (2017). Effectiveness of and overdiagnosis from mammography screening in the Netherlands: population based study. BMJ (Clinical research ed.), 359, j5224.

Bathaie SZ, Ashrafi M, Azizian M, Tamanoi F. (2017) Mevalonate Pathway and Human Cancers. Curr Mol Pharmacol; 10(2):77-85.

Chimento, A., Casaburi, I., Avena, P., Trotta, F., De Luca, A., Rago, V., et al., (2019). Cholesterol and Its Metabolites in Tumor Growth: Therapeutic Potential of Statins in Cancer Treatment. Frontiers in endocrinology, 9, 807.

Grech, G., Zhan, X., Yoo, B. C., Bubnov, R., Hagan, S., Danesi, R, Desiderio, D. M. (2015). EPMA position paper in cancer: current overview and future perspectives. The EPMA journal, 6(1), 9.

Hashemi M, Hoshyar R, Ande SR, Chen QM, Solomon C, Zuse A, Naderi M. (2017). Mevalonate Cascade and its Regulation in Cholesterol Metabolism in Different Tissues in Health and Disease. Curr Mol Pharmacol.10(1):13-26.

Lappano, R., Recchia, A. G., De Francesco, E. M., Angelone, T., Cerra, M. C., Picard, D., & Maggiolini, M. (2011). The cholesterol metabolite 25-hydroxycholesterol activates estrogen receptor α -mediated signaling in cancer cells and in cardiomyocytes. PloS one, 6(1), e16631.

Likus W, Siemianowicz K, Bieńk K, Pakuła M, Pathak H, Dutta C, Wang Q, Shojaei S, Assaraf YG, Ghavami S, et al. (2016) Could drugs inhibiting the mevalonate pathway also target cancer stem cells? Drug Resist Updat. 25:13-25.

Medical Advisory Secretariat (2010). Cancer screening with digital mammography for women at average risk for breast cancer, magnetic resonance imaging (MRI) for women at high risk: an evidence-based analysis. Ontario health technology assessment series, 10(3), 1–55.

Soucek, P., Vrana, D., Ueng, Y. F., Wei, S., Kozevnikovova, R., & Guengerich, F. P. (2018). Selective changes in cholesterol metabolite levels in plasma of breast cancer patients after tumor removal. Clinical chemistry and laboratory medicine, 56(3), e78–e81.