Effects of Chemotherapeutic Agents on Cognitive Function: A Literature Review

Corinne Menz, Dr. Kelly Vowell Johnson and Dr. Hope Ballentine

University of Arkansas

INTRODUCTION

Chemotherapy is commonly the first-line treatment for various types of cancers. However, adverse effects resulting from treatment can negatively impact the patient's quality of life while receiving chemotherapy as well as once the therapy course has been completed. The most commonly experienced effect is chemotherapy-related cognitive impairment (CRCI) and is often referred to as "chemobrain". This review attempts to explore the potential causes of cognitive decline, effects of chemotherapy treatment, and subjective patient reports. Relevant research was compiled in order to understand CRCI and its implications for the care of cancer patients.

METHODS

Data extraction and review of literature was completed using MEDLINE Complete, CINAHL, and PubMed. The key words utilized in the searches included *chemotherapy, cancer, cognitive, cognitive impairment or dysfunction.* The studies needed to meet the inclusion criteria of containing the key words, written in English, and peer-reviewed. Studies were excluded from this review if they were published before 2015 and focused on cancer treatment other than chemotherapy. In total, 12 articles met all of the criteria and were utilized in this review.

RESULTS

Causes of Cognitive Decline

- It is widely believed that the cause of CRCI is multifactorial, with most of the negative effects related to direct neurotoxic effects of chemotherapy, induced hormonal changes, oxidative stress, immune system dysregulation, and vascular damage
- Increased effects of CRCI may be caused by underlying stress, anxiety, and depression

Effects of Treatment

- Using fMRI, there have been depictions of reduction in gray matter in some regions of the brain, while subsequent gray matter volume increases in other areas; this shows that a compensatory mechanism may be occurring to account for the structural changes within the brain.
- However, many of the changes in brain structure were not statistically significant compared to healthy control groups.

Patient Reports

- The Functional Assessment of Cancer Therapy-Cognitive (FACT-Cog) and the Blessed Orientation Memory Concentration Test was used to measure patients' perceived levels of cognitive decline throughout the course of chemotherapy treatment.
- While a large percentage of the patients reported cognitive impairment, it is likely caused by a variety of factors than solely the administration of chemotherapy as evidenced by increase in age, less education, employment status, mental health issues, along with others.

DISCUSSION

It is evident that more research over CRCI needs to be completed. Through conducting this review, it has been found that a variety of factors are at play that impact the development, duration, and severity of cognitive impairment. While many of the studies varied in results, it can be concluded that many patients subjectively report cognitive decline, even if it cannot be objectively measured. Because of this, implications for practice need to be implemented. Development of interventions, both pharmacological and behavioral, should be a priority among providers who give care to patients undergoing treatment. Standardized use of cognitive tests, such as FACT-Cog, can also improve the documentation and occurrence of CRCI, which can promote understanding and proper management of symptoms among these patients. This impairment remains clinically significant and warrants further investigation. Specific causes may be difficult to identify, however more needs to be done to address the issue of CRCI in order to promote optimal patient outcomes.

REFERENCES

Alhareeri, A. A., Archer, K. J., Fu, H., Lyon, D. E., Elswick, R. K., Jr., Kelly, D. L., Starkweather, A. R., Elmore, L. W., Bokhari, Y. A., & Jackson-Cook, C. K. (2020). Telomere lengths in women treated for breast cancer show associations with chemotherapy, pain symptoms, and cognitive domain measures: a longitudinal study. *Breast Cancer Research: BCR*, 22(1), 137. https://doi.org/10.1186/s13058-020-01368-6

Boscher, C., Joly, F., Benedicte, C., Humbert, X., Grellard, J., Binarelli, G., Tron, L., Licaj, I., Lange, M. (2020). Perceived Cognitive Impairment in Breast Cancer Survivors and its Relationships with Psychological Factors. *Cancers*, *12*. https://doi.org/10.3390/cancers12103000

Chen, B. T., Jin, T., Patel, S. K., Ye, N., Ma, H., Wong, C. W., Rockne, R. C., Root, J. C., Saykin, A. J., Ahles, T. A., Holodny, A. I., Prakash, N., Mortimer, J., Waisman, J., Yuan, Y., Li, D., Sedrak, M. S., Vazquez, J., Katheria, V., & Dale, W. (2019). Intrinsic brain activity changes associated with adjuvant chemotherapy in older women with breast cancer: a pilot longitudinal study. *Breast cancer research and treatment*, 176(1), 181-189. https://doi.org/10.1007/s10549-019-05230-y

Costa, D., Loh, V., Birney, D. P., Dhillon, H. M., Fardell, J. E., Gessler, D., Vardy, J. L. (2018). The Structure of the FACT-Cog v3 in Cancer Patients, Students, and Older Adults. *Journal of Pain and Symptom Management*, *55*(*4*), 1173-1178. https://doi.org/10.1016/j.jpainsymman.2017.12.486

Fernandez, H. R., Varma, A., Flowers, S. A., & Rebeck, G. W. (2020). Cancer Chemotherapy Related Cognitive Impairment and the Impact of the Alzheimer's Disease Risk Factor APOE. *Cancers*, *12*(12). https://doi.org/10.3390/cancers12123842

Janelsins, M. C., Heckler, C. E., Peppone, L. J., Kamen, C., Mustian, K. M., Mohile, S. G., Magnuson, A., Kleckner, I. R., Guido, J. J., Young, K. L., Conlin, A. K., Weiselberg, L. R., Mitchell, J. W., Ambronsone, C. A., Ahles, T. A., Morrow, G. R. (2017). Cognitive Complaints in Survivors of Breast Cancer After Chemotherapy Compared with Age-Matched Controls: An Analysis from a Nationwide, Multicenter, Prospective Longitudinal Study. *Journal of Clinical Oncology*, *35*(*5*), 506-514. https://doi.org/10.1200/JCO.2016.68.5826

Kesler, S. R., Petersen, M. L., Rao, V., Harrison, R. A., Palesh, O. (2020). Functional connectome biotypes of chemotherapy-related cognitive impairment. *Journal of Cancer Survivorship*, *14*, 483-493. https://doi.org/10.1007/s11764-020-00863-1

Martin, B. R., Fernandez Rodriguez, E. J., Rihuete Galve, M. I., Cruz Hernandez, J. J. (2020). Study of Chemotherapy-Induced Cognitive Impairment in Women with Breast Cancer. *International Journal of Environmental Research and Public Health*, *17(23)*, 8896. https://doi.org/10.3390/ijerph17238896

Mounier, N. M., Abdel-Maged, A. E.-S., Wahdan, S. A., Gad, A. M., & Azab, S. S. (2020). Chemotherapy-induced cognitive impairment (CICI): An overview of etiology and pathogenesis. *Life sciences*, *258*, 118071. https://doi.org/10.1016/j.lfs.2020.118071

Nakamura, Z. M., Deal, A. M., Nyrop, K. A., Damone, E. M., Muss, H. B. (2020). Associations of functional, psychosocial, and medical factors with cognitive impairment in older, chemotherapy naïve patients with early breast cancer. *Journal of the Psychological, Social, and Behavioral Dimensions of Cancer, 29(8),* 1366-1369. https://doi.org/10.1002/pon.5433

Perrier, J., Viard, A., Levy, C., Morel, N., Allouache, D., Noal, S., Joly, F., Eustache, F., & Giffard, B. (2020). Longitudinal investigation of cognitive deficits in breast cancer patients and their gray matter correlates: impact of education level. *Brain imaging and behavior*, *14*(1), 226-241. https://doi.org/10.1007/s11682-018-9991-0 Piccirillo, J. F., Hardin, F. M., Nicklaus, J., Kallogjeri, D., Wilson, M., Ma, C. X., Coalson, R. S., Shimony, J., Schlaggar, B. L. (2015). Cognitive Impairment after Chemotherapy Related to Atypical Network Architecture for Executive Control. *Oncology*, 2015(88), 360-368. https://doi.org/0.1159/000370117