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Review

Systematic review of pharmacologic and non-pharmacologic interventions to manage cognitive alterations after chemotherapy for breast cancer

Raymond J. Chan [a,b,1], Alexandra L. McCarthy [c,2], Jackie Devenish [d,3], Karen A. Sullivan [e,4], Alexandre Chan [f,g,*]

[a] *Institute of Health and Biomedical Innovation, Queensland University of Technology, Kelvin Grove, Queensland 4059, Australia*
[b] *Cancer Care Services, Royal Brisbane and Women's Hospital, Herston, Queensland 4029, Australia*
[c] *Princess Alexandra Hospital and the Institute of Health and Biomedical Innovation, Queensland University of Technology, Victoria Park Rd, Kelvin Grove, Queensland 4059, Australia*
[d] *The University of Queensland Library Herston Health Sciences Library, Royal Brisbane and Women's Hospital, Herston, Queensland 4029, Australia*
[e] *School of Psychology and Counseling, Queensland University of Technology, Victoria Park Rd, Kelvin Grove, Queensland 4059, Australia*
[f] *Department of Pharmacy, National University of Singapore, Singapore 117543, Singapore*
[g] *Department of Pharmacy, National Cancer Centre, Singapore 117543, Singapore*

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Abstract ***Purpose:*** Cognitive alterations are reported in breast cancer patients receiving chemotherapy. This has adverse effects on patients' quality of life and function. This systematic review investigates the effectiveness of pharmacologic and non-pharmacologic interventions to manage cognitive alterations associated with breast cancer treatment.
Methods: Medline via EBSCO host, CINAHL and Cochrane CENTRAL were searched for the period January 1999–May 2014 for prospective randomised controlled trials related to the management of chemotherapy-associated cognitive alterations. Included studies investigated the management of chemotherapy-associated cognitive alterations and used

* *Corresponding author at:* Department of Pharmacy, National University of Singapore, 18 Science 4, Block S4, Singapore 117543, Singapore. Tel.: +65 6516 7814.
E-mail addresses: Raymond.Chan@health.qld.gov.au (R.J. Chan), al.mccarthy@qut.edu.au (A.L. McCarthy), j.devenish@library.uq.edu.au (J. Devenish), Karen.Sullivan@qut.edu.au (K.A. Sullivan), phaac@nus.edu.sg (A. Chan).
[1] Tel.: +61 7 3646 5833.
[2] Tel.: +61 7 3138 3850.
[3] Tel.: +61 7 3346 4899.
[4] Tel.: +61 7 3138 4609.

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subjective or objective measures in patients with breast cancer during or after chemotherapy. Two authors independently extracted data and assessed the risk of bias.

Results: Thirteen studies involving 1138 participants were included. Overall, the risk of bias for the 13 studies was either high ($n = 11$) or unclear ($n = 2$). Pharmacologic interventions included psychostimulants ($n = 4$), epoetin alfa ($n = 1$) and Ginkgo biloba ($n = 1$). Non-pharmacologic interventions were cognitive training ($n = 5$) and physical activity ($n = 2$). Pharmacologic agents were ineffective except for self-reported cognitive function in an epoetin alfa study. Cognitive training interventions demonstrated benefits in self-reported cognitive function, memory, verbal function and language and orientation/attention. Physical activity interventions were effective in improving executive function and self-reported concentration.

Conclusion: Current evidence does not favour the pharmacologic management of cognitive alterations associated with breast cancer treatment. Cognitive training and physical activity interventions appear promising, but additional studies are required to establish their efficacy. Further research is needed to overcome methodological shortfalls such as heterogeneity in participant characteristics and non-standardised neuropsychological outcome measures.

1. Introduction

Alterations in cognitive function are often observed in patients receiving chemotherapy, particularly those treated for breast cancer [1]. These changes can comprise poor word or name recall, difficulty in staying focused, diminished ability to learn new things and a decreased ability to multitask [2]. Other alterations in executive function, information processing speed, language, motor function and spatial skills are documented. Depending on the nature of the malignancy and the treatment regimen, the time of onset, severity and duration of these changes are highly variable [3], as are its affective, functional and psychosocial outcomes [4].

Depending on the type of cancer investigated, estimates of the prevalence of cancer treatment-related alterations in cognitive function range from 16% to 75% during treatment [5], although they can endure beyond treatment. Supported by findings from neuropsychological tests, reports indicate that individuals can experience longer-term cognitive changes for as long as 21 years after chemotherapy for breast cancer [6]. In addition, imaging research has reported a correlation between deficits in cognitive function and white matter changes in the brain [7].

A number of systematic reviews and meta-analyses have investigated the prevalence of cognitive alteration and its association with treatment in cancer patients [2,8,9]. One systematic review [10] and one non-systematic narrative review, which discussed unpublished and ongoing studies [11], focused on interventions to enhance cognitive function. Both reviews, however, are limited in that they included non-randomised controlled trials. Furthermore, Hines et al. limited their studies to cognitive behavioural therapy (CBT), which does not encompass the full range of interventions available [10]. In summary, a high quality, comprehensive systematic review of interventions for managing chemotherapy-associated cognitive alterations is lacking.

This clinical problem has significant adverse effects on the post-treatment quality of life and function of patients with cancer; hence, interventions to prevent or manage it are warranted. Over the next decade, the number of individuals living with a cancer diagnosis is projected to increase by 31%, with a high proportion being patients with breast cancer [12]. Treatment-associated adverse effects in this growing population have significant public health implications if they are not well managed. In this paper, we systematically review the effectiveness of pharmacologic and non-pharmacologic interventions to manage alterations of cognitive function associated with breast cancer treatment.

2. Method

This systematic review adhered to the PRISMA statement [13] for reporting systematic reviews.

2.1. Search strategy

A medical librarian (JD) searched Medline via EBSCOhost, CINAHL and Cochrane CENTRAL for studies published between January 1999 and May 2014. The key search terms were chemotherapy, antineoplastic agents, chemoradiotherapy, cancer, neoplasms, randomised controlled trial, cognitive impairment, cognitive dysfunction, cognitive disorder, cognitive loss, cognitive deficit and memory disorder. The search was limited to prospective randomised controlled trials (RCTs) published in English that investigated the management of chemotherapy-associated cognitive alterations (as primary or secondary outcomes). Further manual searches of the reference lists of the relevant studies and reviews were undertaken by authors AC, RC and AM.