

Neuropathy as an Adverse Effect of Chemotherapy Diminished After Administration of Dietary Supplement with Iron Citrate – Case Study

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Abstract

Aims: This research examined how adding iron citrate (Synthesit) affected chemotherapy-induced nerve damage in a patient diagnosed with primary fallopian tube cancer.

Methodology: A 51-year-old Lithuanian woman received adjuvant chemotherapy and iron citrate. The blood indices and inflammation markers were monitored.

Results: The patient showed macrocytic normochromic anemia, fluctuating platelet parameters, and varied procalcitonin levels, suggesting Synthesit influences immune function and hematologic parameters during chemotherapy.

Scientific Novelty: This study distinctively investigated the influence of iron citrate on changes in hematologic and immune parameters during chemotherapy.

Conclusion: Synthesit may affect the blood counts, red blood cell production, and immune markers, aiding in chemotherapy-induced neuropathy management.

Keywords: dietary supplements and neuropathy; iron citrate and nerve damage; peripheral neuropathy treatment; neuroprotective supplements in oncology; chemotherapy side effects mitigation.

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Introduction

Primary fallopian tube carcinoma (PFTC), originally described by Rokitansky in 1847, predominantly impacts women aged 60-64 years, especially those postmenopausal [1]. While follicular thyroid papillary carcinoma is often early diagnosed, serous-type epithelial ovarian cancer tends to be detected at more advanced stages [2]. Over 95% of PFTC cases are carcinomas [3], with causes possibly mirroring those of ovarian cancer, involving hormonal, reproductive, and genetic factors. Interestingly, pregnancy, high parity, and oral contraceptive use significantly reduce the risk of PFTC [4]. The prognosis for PFTC is influenced by disease stage, histological subtype, and the success of surgical intervention, with a 34% five-year survival rate in advanced cases [5]. The chemotherapeutic agent carboplatin and paclitaxel are pivotal in the treatment of various cancers, including PFTC. Carboplatin works by forming connections between DNA strands, thereby inhibiting DNA production and repair, while paclitaxel disrupts

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cell division by stabilising tubulin and preventing its disintegration [6-8].

Moreover, the concurrent administration of these therapies exhibits high efficacy and forms the cornerstone of early cancer management strategies [9,10]. Nevertheless, these therapies have severe adverse effects like chemotherapy-induced peripheral neuropathy (CIPN) and myelosuppression that affects between 12% to 96% of patients depending on various risk factors [11-14].

Recent advancements in targeted therapy and immunotherapy offer promising alternatives or adjuncts to traditional chemotherapy, potentially reducing the incidence of CIPN in PFTC treatment. Targeted therapies, including PARP inhibitors and anti-angiogenesis drugs, have demonstrated effectiveness against ovarian and fallopian tube cancers by selectively targeting cancer cell mechanisms, thereby sparing normal cells and mitigating side effects. Immunotherapy, including checkpoint inhibitors, harnesses the body's immune system to fight cancer, providing an additional pathway to enhance patient outcomes and quality of life. These approaches, supported by patient-centred research, suggest a significant enhancement in treatment tolerability and effectiveness, with reduced neuropathy and better overall quality of life.

When patients are suffering from CIPN, duloxetine and venlafaxine are commonly employed due to their capacity to alleviate pain in patients following administration; however, it is important to note that duloxetine is normally administered at 60mg per day. This has been caused by an increase in the number of alternative strategies which include physical therapy, yoga, acupuncture, cryotherapy, compression therapy and neurofeedback among others as shown by their increasing tailoring to suit individual needs indicating a shift towards more holistic approach in this particular area of treatment [16,17].

Duloxetine must be used in the treatment and management of chemotherapy-induced peripheral neuropathy. There is no available evidence to show that duloxetine should be discontinued during the initial stages of CIPN. For this reason, it is important for the oncologist to continue using duloxetine as part of the patients' therapy. In cases of severe neuropathy, modifications may be necessary in the chemotherapy regimen. Although acupuncture and physical therapy are adjunct treatments that have been found useful in some cases [18] ongoing studies aim to establish the therapeutic efficacy of these interventions [9]. Dietary supplements are also considered potential treatments for chemotherapy-induced peripheral neuropathy, one such compound being iron citrate which may greatly enhance the life quality during the treatment [19]. Other supplements include B and D vitamins, zinc, magnesium curcumin, and St John's Wort among others which hold promise for relief from neuropathic pain [20]. Research focused on restoring neuronal iron homeostasis represents a potential avenue for promoting neurogenesis or axonal and neuronal regeneration following spinal cord injury, offering potential benefits for cancer patients affected by chemotherapy-induced peripheral neuropathy (CIPN) [21].

The integration of targeted therapies and immunotherapies into the treatment paradigm for PFTC holds great promise. This approach not only enhances treatment efficacy but also contributes to the reduction in both incidence and severity of chemotherapy-induced peripheral neuropathy (CIPN), illustrating a comprehensive approach to cancer care that prioritises patient well-being alongside clinical outcomes.

Case Presentation

Background

The case report centered on a 51-year-old Lithuanian woman diagnosed with right-sided fallopian tube cancer. At first, acute abdomen occurred in May 2020 and ultrasonography showed an 8 cm mass near the right ovary. Later, laparoscopy confirmed of a high-grade poorly differentiated fallopian tube carcinoma pT1a. In addition, other explorations conducted during October 2020 led to findings of uterine fibroids, liver haemangioma as well as cysts in her right kidney. A laparoscopic procedure in March 2021 encompassed total hysterectomy, right adnexectomy, appendectomy, omentectomy, and para-aortic lymph node removal. The post-operation, adjuvant chemotherapy with carboplatin and paclitaxel resulted in the emergence of such consequences that led to both single-agent carboplatin and Synthesit containing iron citrate. Astonishingly, neuropathy and peripheral numbness were notably mitigated by Synthesit while at the same time, it assisted in the restoration of chemotherapy-induced anemia.

The case underscored the complexity of cancer treatment, emphasizing the absence of a universal approach. Previous interventions successfully prevented hypersensitivity reactions, and ondansetron was administered to manage emesis induced by carboplatin. Transitioning to monotherapy alleviated treatment burden without compromising efficacy. The fact that inappropriate effects were suitably controlled from this moment onwards made it clear about the importance of personalised collaborative care for patient's adverse response planning which culminated in introduction of Synthesit. The case demonstrated a personal, holistic approach to cancer therapy through incorporation of complementary mechanisms aimed at improving the effectiveness of treatment outcomes as well as enhancing patients' well-being.

Research Problem

However, despite the progress in cancer therapy, chemotherapy-induced neuropathy still poses a number of problems for patients' well-being. Currently, many management strategies are ineffective in adequately addressing neuropathic symptoms, necessitating exploration of alternative approaches. Therefore, there is need to investigate the effectiveness of dietary supplementation with iron citrate as an adjunctive treatment in order to optimise symptomatology and improve patient outcomes resulting from chemotherapy-induced neuropathy.

Objectives

To determine the efficacy of iron citrate dietary supplementation in reducing the severity of chemotherapy-induced neuropathy symptoms, this study employed pain scores, functional impairment assessments, and measures of neuropathy-related quality of life as indicators.

Results

Table 1 presents the changes in white blood cell parameters before and after Synthesit intake from June 1, 2021, to July 13, 2021. The parameters include leukocytes, neutrophils, lymphocytes, monocytes, eosinophils, and basophils, measured in units of $\times 10^9/l$ (count per liter) or as a percentage. For each parameter, the values recorded before taking Synthesit, during two phases of Synthesit intake, and the corresponding reference range where applicable. The changes in these parameters indicate the impact of Synthesit on the patient's white blood cell counts and distribution, which are essential indicators of immune system function. Overall, the table facilitates an assessment of how Synthesit may have influenced the patient's immune response during the specified period.

Table 1. Blood white cells parameters changes before and after using Synthesit (from 1. June 2021 to 13. July 2021)

Parameter (unit of measurement)	Before Synthesit intake 1.6.2021	During Synthesit intake 22.6.2021	During Synthesit intake 13.7.2021	Reference Range
Leukocytes ($\times 10^9/l$)	5.18	3.71	3.69	4.0 - 9.08
Neutrophils (%)	49.70	34.90	24.00	40 - 65
Lymphocytes (%)	42.10	56.10	66.00	25 - 37
Monocytes (%)	6.90	6.20	8.10	2 - 10
Eosinophils (%)	0.60	2.50	0.90	0 - 5
Basophils (%)	0.70	0.30	0.40	0 - 1
Neutrophils ($\times 10^9/l$)	2.60	1.30	0.90	1.5 - 6.0
Lymphocytes ($\times 10^9/l$)	2.20	2.10	2.50	1.0 - 4.0
Monocytes ($\times 10^9/l$)	0.40	0.20	0.30	0.1 - 0.9
Eosinophils ($\times 10^9/l$)	0.00	0.10	0.00	0.0 - 0.7
Basophils ($\times 10^9/l$)	0.00	0.00	0.00	0.0 - 0.11

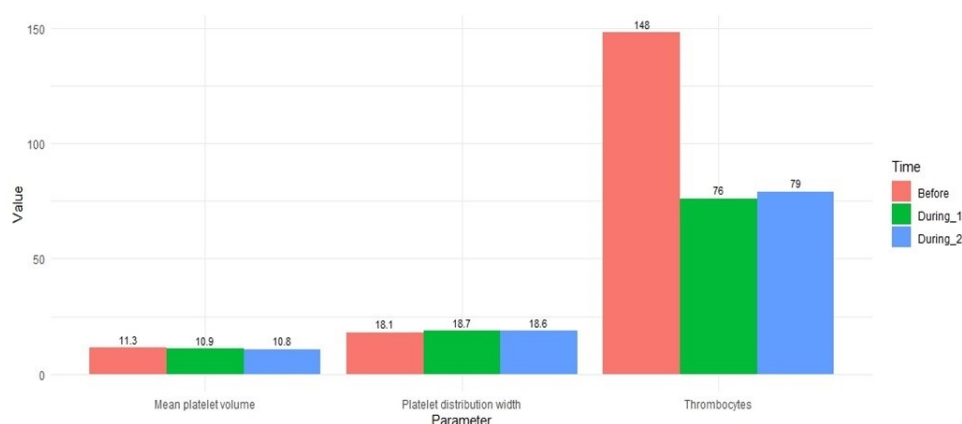
All this demonstrates that Synthesit intake led to observable changes in white blood cell parameters, including leukocytes, neutrophils, lymphocytes, monocytes, eosinophils, and basophils. These changes suggest a potential impact on the patient's immune system, reflecting variations in immune response and white blood cell distribution over the treatment period. Table 2 provides an overview of the changes in red blood cell parameters before and after Synthesit intake from June 1, 2021, to July 13, 2021. Some of the parameters measured in an FBC include erythrocytes, nucleated red blood cells (NRBC), haemoglobin, mean corpuscular volume (MCV), erythrocytes, red cell distribution width - standard deviation (RDW-SD), MCH concentration and MCH. They are measured using different units such as counts per liter ($\times 10^9/l$), percentage (%), grams per liter (g/l) and Liters per Liters (l/l). Additionally, the table includes the reference range for each parameter, facilitating the comparison of the patient's values against the normal range. The changes observed in these parameters offer insights into the effects of Synthesit on red blood cell count, size, and haemoglobin content, as well as the overall distribution of red blood cells in the patient's bloodstream.

Table 2. RBC parameters change before and after using Synthesit (from 1. June 2021 to 13. July 2021)

Parameter (unit of measurement)	Before Synthesit intake 1.6.2021	During Synthesit intake 22.6.2021	During Synthesit intake 13.7.2021	Reference Range
Nucleated erythrocytes (x/100WBC)	0.00	0.00	0.20	0.00
NRBC (x10 ⁹ /l)	0.00	0.00	0.01	0.00
Erythrocytes (x10 ¹² /l)	3.58	3.11	3.22	4.1 – 5.1
Haemoglobin (g/l)	122.00	109.00	117.00	114 – 145
Haematocrit (l/l)	0.36	0.32	0.337	0.36 – 0.42
Mean corpuscular volume (fl)	101.40	102.80	104.90	78 – 96
Mean corpuscular haemoglobin (pg)	34.00	34.90	36.30	26 – 31
MCH concentration (g/l)	335.00	340.00	346.00	310 – 370
Red cell distribution width - SD (fl)	59.50	67.80	73.10	39.0 – 51.5

These highlights significant changes in red blood cell parameters before and after Synthesit administration from June 1, 2021, to July 13, 2021. The comparison against reference ranges indicates Synthesit's impact on red blood cell count, size, hemoglobin content, and distribution, suggesting potential improvements in hematologic health.

Figure 1 depicts the changes in Platelet Parameters before and after Synthesit intake from June 1, 2021, to July 13, 2021. The x-axis represents the different time points of measurement, including "Before taking Synthesit," "During taking Synthesit (June 22, 2021)," and "During taking Synthesit (July 13, 2021)." The y-axis indicates the values of the red blood cell parameters measured in the respective units (x10⁹/l for Thrombocytes, fl for Mean platelet volume and Platelet distribution width). Each parameter (Thrombocytes, mean platelet volume, and Platelet distribution width) is represented by a different color bar, and the height of each bar corresponds to the measured value at each time point. The reference ranges for each parameter are also provided for context. The figure visually illustrates the changes in these red blood cell parameters over the specified time period in relation to the reference ranges, providing insights into the impact of taking Synthesit on these parameters.

**Figure 1. Platelet Parameters changes before and after taking Synthesit from 1. June 2021 to 13. July 2021**

These results showed that Synthesit intake from June 1, 2021, to July 13, 2021, resulted in noticeable changes in platelet parameters (Thrombocytes, Mean Platelet Volume, and Platelet Distribution Width). The data indicated variations within and outside the reference ranges, suggesting Synthesit's impact on platelet characteristics.

Figure 2 illustrates the changes in the inflammatory marker (Procalcitonin) before and after taking Synthesit from June 1, 2021, to July 13, 2021. The x-axis represents the time points at which measurements were taken: "Before," "During," and "During" again. The y-axis denotes the levels of Procalcitonin measured in percentage (%). The plot shows a decrease in Procalcitonin levels from 0.17% before taking Synthesit to 0.08% during the first phase of Synthesit intake. However, during the subsequent phase of Synthesit intake, the Procalcitonin levels slightly increased to 0.09%. These changes are compared against the reference range for Procalcitonin, which is typically between 0.15% and 0.35%. Overall, the figure demonstrates the fluctuation of Procalcitonin levels before and after taking Synthesit within the context of the reference range.

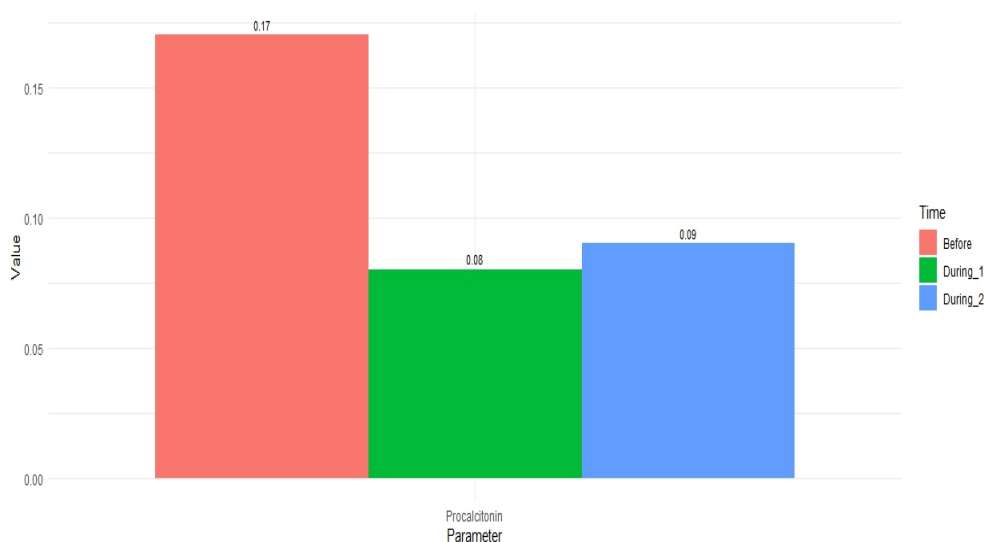


Figure 2. Inflammatory Marker changes before and after taking Synthesit from 1. June 2021 to 13. July 2021

These findings showed that initial intake of Synthesit reduced Procalcitonin levels from 0.17% to 0.08%. However, with continued use, levels slightly increased to 0.09%. Despite fluctuations, Procalcitonin levels remained below the reference range (0.15%-0.35%), suggesting Synthesit might help lower inflammation markers.

Discussion

The case study highlighted notable alterations in white blood cell parameters following Synthesit (Iron citrate) administration from June 1, 2021, to July 13, 2021. Contrary to expectations of lymphocytopenia during anti-cancer drug therapy, a higher percentage of lymphocytes was observed. Possible contributing factors to this observation include decreased neutrophil counts and the use of corticosteroids. Chronic infections like Epstein-Barr virus may also influence lymphocyte levels. These shifts suggest an impact on immune function, yet caution is advised in interpretation, considering individual health conditions. However, another study demonstrated that it's crucial to interpret these findings within the broader context of clinical significance and individual health conditions [22]. To fully understand how it affects white blood cells, more scrutiny is needed on Synthesit. Research in the future has to concentrate on matters of prescription for medical purposes as regards quantity, timing and safety.

From the period of June 1 to July 13, 2021, a post-Synthesit supplementation analysis found some interesting changes in hematological parameters like reduced hematocrits, normalisation of hemoglobin levels and MCV, MCH and nucleated red blood cells increased all indicating a possible macrocytic anemia. However, as concerns interpretation of these findings, absence of B vitamins makes it difficult because deficiency in these vitamins might result in macrocytic anemia. High RDW values detected also indicate that there was/is anisocytosis among the persons studied. These findings are important; nonetheless other possible causes such as iron deficient anemia, folate deficient anemia and vitamin B12 deficient anemia can influence RBC parameters [23]. There are also other conditions such as hemolysis that may cause similar changes [24]. Furthermore, things like storage methods used for blood samples and influence of some drugs including oral antidiabetics that can alter outcomes found out [25]. Besides, there is need for caution concerning chronic inflammation and oxidative stress which contribute to non-enzymatic glycation as well as interferes with the fluidity of cell membranes [26]. Synthesit can therefore affect RBC indices, but these parameters have other interfering factors which should be considered before any conclusions are made. Other plausible avenues merit exploration to determine the reasons behind the observed fluctuations in blood counts; this evidence underscores the multifaceted nature of factors influencing RBC indices. This is important information if one is to be in a position to develop new therapeutic interventions that take into consideration various influences especially in cases of chemotherapy related scenarios.

The study revealed that the indexes of thrombocytes that included thrombocytes count, mean volume of platelets and platelet variability known as platelet distribution widths were elevated with Synthesit use. While comparing carboplatin with cisplatin it was observed that carboplatin induced thrombocytopenia during the third course of CHOP making it obligatory to check thrombocytes level and possibly decrease the dose. Additionally, it is believed that MPV and PDW play a role in Acute Coronary Syndrome, chronic kidney disease liver cirrhosis and autoimmune diseases [27]. Since the platelet activation can cause functional changes of the parameters, then the changes of such parameters should be associated with activation [28]. Consequently, these variations in platelet parameters under Synthesit influence could be direct effects of the drug itself or already existing conditions or drug interferences.

Certain diseases exhibit associations with variations in platelet indices such as mean platelet volume (MPV) and platelet distribution width (PDW), including acute coronary syndrome, chronic kidney disease, liver cirrhosis, and

autoimmune disorders. The aforementioned variations may arise from the effects of medications, underlying diseases as well as interactions such as those seen with carboplatin. Future research should prioritise strategies for preventing chemotherapy-induced peripheral neuropathy and investigate their implications for clinical management. This research highlighted the need for inventive protocols of managing chemotherapy that minimise the adverse impacts of chemotherapy on patients' lives. Furthermore, it suggested that nitric oxide/cytokine interactions could modulate procalcitonin levels by way of inflammatory immune responses which have implications for pain relief/procalcitonin secretion through neuroendocrine responses. Such insights may help developing novel approaches leading to control inflammation and pain in clinical settings using these pathways.

This report presented valuable implications for future medicine as well as the development of novel therapy modalities for chemotherapy-induced conditions. By expanding the knowledge about the influence of Synthesit and other medicines in affecting various hematological and platelet indices, treatment protocols can be refined that will help better manage side effects associated with chemotherapy thereby enhancing patient outcomes and advancing clinical practice.

Conclusions and Implications

The case study showed the possible advantages of administering a patient suffering from neuropathy iron citrate, as indicated by a decrease in neuropathy symptoms and an improvement in general body health during chemotherapy. However, further studies are necessary to fully understand the underlying mechanisms affecting both symptom management and hematological parameters. Other than just managing peripheral neuropathy, this can be done through careful examination of the wider implications for iron citrate supplementation when used in cancer treatment settings. Consequently, these results highlight the necessity of evaluating complementary strategies linked to chemotherapy-induced peripheral neuropathy such as using iron citrate supplements aimed at increasing patients' life quality. The ongoing research about its mechanisms and other ways it could be used contribute to better symptom management plans or strategies and thus, successful treatment approaches for people who have cancer. There is also a need to monitor the administration and adjust doses of iron citrate in order to achieve desired therapeutic effect without causing harm to a patient. Research in this area is crucial as it has the potential to streamline symptom management, enhance patient well-being, and optimize the overall treatment outcomes for cancer patients undergoing chemotherapy. The impacts of iron citrate supplementation on neuropathic symptoms and its potential to affect the management of these symptoms cannot be overlooked. Consequently, more research needs to be conducted in order to establish its mechanisms as well as its broad applications so as to improve treatment strategies for cancer patients who have neuropathy.

Declarations

Authorship Contribution

Conceptualization: Patrik Kusnir; data curation: Shahbaz Baig; formal analysis: Patrik Kusnir; research: Patrik Kusnir, Shahbaz Baig; methodology: Patrik Kusnir; project management: Shahbaz Baig; resources: Shahbaz Baig; software: Shahbaz Baig; supervision: Patrik Kusnir; validation: Patrik Kusnir; display: Shahbaz Baig; drafting - original draft: Patrik Kusnir; writing - proofreading and editing: Shahbaz Baig.

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Regarding the publication, the author states that there is no conflict of interest.

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