SZYMAŃSKI, Bartłomiej, PIASZCZYŃSKI, Szymon, PŁESKA, Kacper, WOJTANIA, Joanna, ŁEPIK, Michał, USZOK, Zofia, ROSIAK, Krzysztof, REGUŁA, Kacper, WALOCH, Kamil and CZAJKA, Andrzej. The impact of chemotherapy dose adjustment and delay in patients with leukemias and lymphomas who exercise. Quality in Sport. 2024;21:51462. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.21.51462
https://apcz.umk.pl/QS/article/view/51462

The journal has had 20 points in Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 17.05.2024. Revised: 25.05.2024. Accepted: 29.05.2024. Published: 05.06.2024.

The impact of chemotherapy dose adjustment and delay in patients with leukemias and lymphomas who exercise

Bartłomiej Szymański Norbert Barlicki Memorial Teaching Hospital no. 1 of the Medical University of Lodz, Dr. Stefana Kopcińskiego 22, 90-153 Lodz, Poland
https://orcid.org/0009-0006-8915-0364
szymanski.b458@gmail.com

Szymon Piaszczyński, Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland
https://orcid.org/0009-0007-8600-2339
szpiaszczynski@gmail.com

Kacper Płeska, Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland
https://orcid.org/0000-0001-8495-8766
pleskakacper@gmail.com

Joanna Wojtania, Independent Public Health Care Facility of the Ministry of Internal Affairs and Administration, ul. Polnocna 42, 91-425 Lodz, Poland
https://orcid.org/0009-0006-3466-8860
joanna.wojtania@outlook.com
Michał Łepik, Military Medical Academy Memorial Teaching Hospital – Central Veterans' Hospital, ul. Zeromskiego 113, 90-549 Lodz, Poland
https://orcid.org/0009-0005-5441-2005
michal.lepik2@gmail.com
Zofia Uszok, Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland
https://orcid.org/0009-0002-2111-8094
zofia.uszok@stud.umed.lodz.pl
Krzysztof Rosiak, Military Medical Academy Memorial Teaching Hospital – Central Veterans' Hospital, ul. Zeromskiego 113, 90-549 Lodz, Poland
https://orcid.org/0009-0007-8536-9809
krzysztof.rosiak15@gmail.com
Kacper Reguła, County Hospital of Zawiercie, ul. Miodowa 14, 42-400 Zawiercie, Poland
https://orcid.org/0009-0001-5291-7043
kacfilreg@gmail.com
Kamil Waloch, Medical University of Lodz, al. Tadeusza Kosciuszki 4, 90-419 Lodz, Poland
https://orcid.org/0009-0003-0697-1393
kamilwaloch7@gmail.com
Andrzej Czajka, Provincial Specialized Hospital in Zgierz Parzęczewska 35, 95-100 Zgierz, Poland
https://orcid.org/0009-0008-8888-3982
andrzej.czajka0509@gmail.com

Abstract

This review addresses the critical challenge of leukemia and lymphoma, delving into the epidemiology, treatment adherence, impact of physical activity, and the pressing need for more effective chemotherapy protocols. The purpose is to synthesize current knowledge, highlight existing gaps, and emphasize the importance of innovation in patient care strategies.

Epidemiological data show variability in incidence rates and underscore the roles age, genetics, and lifestyle play in disease risk and progression. These insights are vital for effective prevention and timely intervention.

The focus of the discussion revolves around the development of chemotherapy protocols. Tailoring these to the individual's genetic and cancer profile can lead to significant gains in efficacy and minimize unwanted side effects, crucially improving patient quality of life and compliance.

Treatment adherence is fundamental to successful outcomes, requiring multifaceted support strategies. Education, side-effect management, and addressing care barriers are pivotal in ensuring patients fully benefit from therapy. Personalization in chemotherapy protocol development is a current focus, aiming to maximize efficacy while minimizing side effects to improve quality of life and survival. The conclusion advocates for an integrated approach combining research and clinical practice to cater to the biological intricacies of both the malignancy and the patient. Progress in these areas proclaims a future where personalized, effective, and compassionate cancer treatment is the norm, pushing us closer to the goal of transforming cancer into a manageable condition.

Review methods

A review of the literature from PubMed and Google Scholar (1980-2023) was conducted. The articles were selected based on specific keywords and then evaluated for their significance and suitability for inclusion in this review.

Keywords : Chemotherapy, delays, oncology, physical activity, leukemia, lymphoma

Epidemiology

Leukemia and lymphoma are both types of blood cancers, but they affect the body in different ways and have distinct epidemiological profiles.

Leukemia involves the bone marrow and causes the production of abnormal white blood cells, which can disrupt normal blood cell function and spread into the bloodstream. It is classified into four main types: Acute Lymphoblastic Leukemia (ALL), Chronic Lymphocytic Leukemia (CLL), Acute Myeloid Leukemia (AML), and Chronic Myeloid Leukemia (CML).

ALL is predominantly a childhood disease, responsible for 80% of leukemia cases in children. The incidence peaks between 2 and 5 years of age. Although less prevalent among adults, the prognosis is typically worse.[1]

CLL is the most common form of leukemia in adults in Western countries, typically impacting individuals over 50 and being rare among children. The disease often progresses slowly, allowing many patients to live for several years with the condition.

AML is more common in adults and its incidence increases with age. It involves the rapid growth of abnormal white blood cells that gather in the bone marrow, hindering the production of normal blood cells.

CML primarily affects adults, typically diagnosed around the age of 65. The prognosis and survival of CML patients have seen significant improvement with the introduction of tyrosine kinase inhibitors.[2]

The incidence of leukemia accounts for a significant proportion of cancer diagnoses, particularly among children, where it is one of the most common types of pediatric cancers. ALL is the most common form of cancer in children and has a very high survival rate when treated appropriately. In adults, the incidence rates increase with age. The rates of leukemia vary globally, with differences observed between countries and within different population groups.[3]

Survival rates for leukemia have improved over the past few decades, particularly for certain types such as childhood ALL, where the 5-year survival rate is now approaching 90%.[4] This success is attributed to advances in chemotherapy protocols and supportive care. However, survival rates can still vary based on factors such as age at diagnosis, leukemia subtype, and the presence of certain genetic mutations.

Leukemia risk factors can include a combination of genetic and environmental elements. For example, exposure to ionizing radiation, certain chemicals like benzene, and previous

chemotherapy or radiation therapy can increase the risk of leukemia.[5][6][7] A small percentage of leukemias are associated with genetic disorders such as Down syndrome.

In 2019, the global number of incident cases, deaths, and disability-adjusted life years from leukemia stood at 0.64 million, 0.33 million, and 11.66 million, respectively. The study projected these rates through to 2030, noting significant global variation.[8]

Lymphoma epidemiology encompasses the study of the incidence, distribution, and possible control of this type of blood cancer. Lymphoma is not a single disease but rather a group of several subtypes, primarily divided into Hodgkin's lymphoma and non-Hodgkin's lymphoma.

Hodgkin's Lymphoma:

The incidence of Hodgkin's lymphoma varies worldwide, with higher rates observed in developed countries compared to developing regions. It accounts for about 0.5% of all cancers diagnosed annually.

HL has a bimodal age distribution, meaning there are two incidence peaks: one in young adulthood (around 20-30 years old) and another in later life (over 55 years old).

Risk factors include a history of Epstein-Barr virus infection, a family history of HL, age, sex (slightly more common in males), and HIV infection. [9]

Due to effective treatment options, the 5-year survival rate for HL can be as high as 90% if diagnosed early. Even in cases with advanced HL, the prognosis can be favorable with current treatment protocols. [10]

Non-Hodgkin's Lymphoma:

NHL is more common than HL and represents a diverse group of malignancies with varying behavior and treatment responses. It ranks among the top ten types of cancer in frequency and is on the rise in many countries, partly due to an aging population. Additionally, it stands as the sixth leading cause of cancer-related deaths in the United States. [11]

Most patients with NHL are diagnosed in their 60s and 70s, although some subtypes affect children and young adults.[12]

There are over 60 subtypes of NHL with vastly different prognoses, the most common being diffuse large B-cell lymphoma and follicular lymphoma. Subtypes can vary significantly concerning their aggressiveness, originating cell type, and clinical presentation.

Potential risk factors for NHL include older age, male sex, Caucasian ethnicity, autoimmune diseases, infectious agents (like HIV, HTLV-1, and H. pylori), immunosuppression, and exposure to certain chemicals like pesticides, and certain medical treatments including chemotherapy and radiation.

Outcomes for NHL vary widely depending on the subtype, stage at diagnosis, and patient factors, with the overall 5-year survival rate around 70%. Survival rates have improved but are lower than those for HL, with 5-year survival rates ranging significantly based on specific characteristics of the disease.[13]

Geographically, the incidence of lymphomas can vary and is influenced by factors such as infectious agents, lifestyle, environmental exposures, and genetic predisposition. Regional collaborative initiatives have

Background on chemotherapy in hematologic malignancies

Chemotherapy is a fundamental treatment modality for hematologic malignancies, which include a broad class of cancers such as leukemias, lymphomas, and multiple myeloma. These malignancies originate in the blood-forming tissues of the body; hence, systemic therapies like chemotherapy are essential for their management.

At its core, chemotherapy works by targeting and destroying rapidly dividing cells, which is a characteristic of cancerous cells.[14] It can be delivered through various routes such as orally or intravenously, and treatment regimes can be single-agent or combination therapies, tailored to the specific type and stage of cancer.

The reasoning behind chemotherapy in treating blood cancers lies in its potential to induce remission. For acute leukemias, chemotherapy aims to achieve complete remission where no disease is detectable. In chronic leukemias or lymphomas, the goal may be to control the disease, prolong survival, and improve quality of life. However, the effectiveness of chemotherapy in hematologic malignancies is not without challenges.[15]

The dosing and scheduling of chemotherapy drugs are determined through rigorous clinical trials that establish the optimal balance between efficacy and toxicity. These regimens serve as standardized guidelines that aim to eradicate malignant cells and prevent the progression of the disease while preserving as much normal function as possible.

Dosing schedules are crucial in this form of treatment. They are designed around the biology of the cancer and the patient's capacity to tolerate and metabolize the drugs. The timing of the treatments is crucial as it enables the optimal destruction of cancer cells while allowing sufficient time for the body to recuperate before the next dose.

Despite these carefully calibrated plans, variations in actual chemotherapy administration can occur. Factors such as drug toxicity, patient comorbidities, and individual responses to chemotherapy may necessitate adjustments to the treatment regimen. Patients with hematologic malignancies might undergo dose reductions or experience treatment delays, particularly when faced with complications such as neutropenia—a deficiency of white blood cells, which makes patients more susceptible to infections.[16]

The complexity of these treatment regimens and their critical role in patient outcomes highlights the importance of adhering to prescribed chemotherapy dosing protocols. Yet, the reality of clinical practice sometimes departs from the ideal scenarios presented in clinical trial protocols. Physical activity can help reduce the negative effects of chemotherapy

In this context, it is essential to understand the full implications of chemotherapy dose modifications in the treatment of hematologic cancers. Such an understanding can guide various stakeholders, including healthcare providers, patients, and policymakers, to collaboratively improve treatment approaches and maximize patient outcomes while ensuring safety and quality of life.

Stages of chemotherapy in hematologic malignacies

Induction Chemotherapy

The initial phase is aimed at inducing a complete remission of the disease. In acute leukemias, this entails aggressive treatment to kill as many cancer cells as possible and reduce the tumor burden to undetectable levels. This stage often involves high doses of chemotherapy and is typically the most intense phase of treatment.

Consolidation (or Intensification) Chemotherapy

Once remission is achieved, the consolidation phase seeks to eliminate any remaining undetected disease, thereby preventing relapse. This stage may involve the same drugs used during induction, different drugs, or a combination, administered at full or reduced doses depending on the patient's response and the level of remaining disease.

Maintenance Chemotherapy

In some hematologic cancers, particularly certain types of lymphoma and chronic leukemias, maintenance therapy is used after the disease has been brought under control. The goal is to maintain remission and prolong the duration of disease-free survival. Maintenance can be less aggressive than induction or consolidation and often continues for months or years.

Common challenges in treatment adherence

Adherence to chemotherapy regimens in the treatment of leukemias and lymphomas presents unique challenges due to the nature of the diseases, the intensity of the treatment protocols, and the individual circumstances of patients. Below are some of the common challenges to treatment adherence specifically in the context of leukemias and lymphomas:

1. Intensity of Treatment

Leukemias and lymphomas often require aggressive chemotherapy protocols that can be physically and emotionally taxing for patients. The rigorous nature of the treatment, including induction and consolidation phases, can lead to higher incidences of severe side effects such as neutropenia, thrombocytopenia, anemia, nausea, vomiting, and fatigue.[17]

2. Comorbidities

Patients with concurrent health issues may have a harder time tolerating chemotherapy and may require adjustments to their treatment regimens to accommodate their overall health status. [18]

3. Psychosocial Factors

Emotional, psychological, and social factors can significantly impact a patient's ability to adhere to treatment. These can include depression, anxiety, lack of social support, or the psychological toll of a cancer diagnosis and ongoing treatment.

4. Financial and Economical Burdens

The high cost of treatment can also be a barrier to adherence, as patients may struggle with expenses related to their treatment, including medication costs, transportation to and from the treatment center, and loss of income.

5. Health System Inefficiencies

Limited access to healthcare facilities, long waiting times for treatment, and a lack of seamless care coordination can lead to missed or delayed chemotherapy sessions.

6. Patient-Provider Communication

Poor communication between patients and healthcare providers can result in misunderstandings about the necessity of strict adherence to treatment schedules and the seriousness of side effects, leading to suboptimal treatment.

7. Medication Complexity

The complexity of chemotherapy regimens, with multiple medications and precise dosing schedules, can be overwhelming for patients, particularly in the absence of adequate education and support systems.

8. Cognitive Factors

Patients may forget doses or have difficulty understanding their treatment regimen, especially if they have cognitive impairments or low health literacy. It is common knowledge that patients who exercise show greater cooperation during treatment.

Understanding and tackling these challenges are essential for improving adherence and consequently, treatment outcomes. This involves multi-disciplinary strategies including patient education, social and emotional support services, financial counseling and healthcare

system improvements aimed at facilitating access to care and simplifying treatment protocols where possible. Collaborative efforts between patients, healthcare providers, and the broader healthcare system play a crucial role in enhancing adherence to chemotherapy treatment regimens.

Impact of Dose adjustment

The relative dose intensity quantifies the administered chemotherapy dose and schedule against standard recommendations, reflecting modifications in treatment due to delays, dose reductions or omitted cycles. Evidence indicates that upholding the RDI correlates with better patient outcomes. In aggressive non-Hodgkin lymphoma specifically, a consistent RDI is a significant and independent marker of achieving complete remission and overall survival. Maintaining the relative dose intensity of chemotherapy is crucial for optimal treatment outcomes.[19][20]

Lower RDI can lead to a reduced rate of complete response, meaning that the chemotherapy may not fully eradicate the cancer cells. This is paramount as achieving a complete response is often correlated with the best prognosis for patients.

Furthermore, overall survival is a key measure of treatment success, and data indicates that patients with a lower RDI have shorter survival times. This suggests that the intensity and consistency of the treatment are essential for prolonging life and improving the chances of long-term remission.

In addition to impacts on complete response and survival, a lower RDI has been linked to an increased probability of the disease progressing or returning after an initial response to treatment. This is especially concerning as it could mean that despite initial treatment efforts, the lymphoma remains active and may continue to grow or spread, necessitating additional treatments which may be more intensive and with their own attendant risks and side effects.[21]

In the high-risk group of patients with acute lymphoblastic leukemia, the study found that an interval before the 8th day of treatment significantly impacted patient outcomes. Specifically, delaying treatment until after the 8th day resulted in a substantial decrease in the 5-year overall survival (5-year OS) by 44.1% and in the 5-year event-free survival (5-year EFS) by 48.6%.[22] However provided excerpts from the article do not include specific data regarding

the statistical significance of differences in 5-year overall survival and event-free survival for patients experiencing chemotherapy intermission before the 15th or 33rd day of treatment compared to those without such delays. This data clearly indicates that early treatment delays are particularly detrimental for patients categorized as high risk, emphasizing the critical importance of timely initiation of chemotherapy in this group to improve survival chances.

In a retrospective study by Bowhay-Carne et al.,[23] it is important to consider the specific findings and the broader context of oncology treatment when evaluating the lack of correlation between chemotherapy relative dose intensity and treatment efficacy.

The study conducted a retrospective analysis of two patient cohorts treated for Hodgkin lymphoma with ABVD combination chemotherapy and for diffuse large B cell lymphoma with RCHOP-21. It found that variances in RDI did not significantly impact treatment outcomes, such as remission rates. Univariate analysis across different RDI categories (>90%, 80-89%, and <80%) showed no significant differences in their respective treatment outcomes.

This lack of observed correlation challenges the traditional belief that maintaining full chemotherapy RDI is critical for achieving the best possible outcomes. Instead, the findings suggest that for patients with these specific types of lymphoma, some flexibility in chemotherapy dosing does not compromise the cure.

It is important to highlight that while the study's results indicate no substantial difference in efficacy across RDIs, this does not negate the importance of striving for optimal dosing. The conclusions are drawn from retrospective data, which inherently cannot control for all variables and potential confounding factors. Moreover, the study itself acknowledges the need for further research to pinpoint the threshold at which reduced RDI could become detrimental to patient outcomes.

It’s also crucial to consider the patient's individual context. The study observed a correlation between higher comorbidity index scores and lower average RDI in the Hodgkin lymphoma cohort. This reflects a nuanced view that treatment must be personalized accounting for the patient’s overall health and RDI adjustments may be necessary and justified in certain clinical scenarios without negatively impacting results.

In summary, the argument against a stringent adherence to full RDI, based on this single study, rests on the premise that slight decreases in RDI did not significantly affect the cure rates for

the HL and DLBCL patient cohorts examined. However, it is a preliminary finding and should not be extrapolated broadly until further studies corroborate these results. Clinicians must continue to weigh the benefits and risks of RDI adjustments on a case-by-case basis, always considering the best interest and safety of their patients.

Positive implications of dose adjustment

While the aim in chemotherapy is often to maintain dose intensity, there are certain circumstances where dose adjustments and delays can have positive implications for patient care. Adjusting the dosage can help manage both acute and chronic toxicities associated with chemotherapy, thereby enhancing the patient's quality of life and their willingness to continue treatment. It allows physicians to tailor treatment protocols to the individual patient, considering their unique physiological responses and personal circumstances.

By carefully calibrating the treatment regimen, healthcare providers can improve the tolerability of chemotherapy, potentially increasing the patient's adherence and likelihood to complete the full course of therapy. Such modifications can also be essential for patients with comorbidities or those experiencing severe adverse reactions; in these cases, reducing the chemotherapy dose or introducing treatment breaks can prevent serious complications and enable patients to recover adequately between treatment cycles.[24]

Moreover, treatment delays can sometimes provide an opportunity for medical teams to evaluate the cancer's response to therapy and make informed decisions about the course of treatment moving forward. In scenarios where ongoing chemotherapy threatens to impair critical organ functions, reducing the dose may preserve these functions and still provide a therapeutic benefit.

Ultimately, any decision to adjust chemotherapy doses or schedule treatment delays must weigh the advantages of reduced side effects and improved patient comfort against the potential impact on the overall effectiveness of the cancer treatment. These decisions are carefully considered in a complex context, weighing the clinical evidence and the patient's individual experience during their course of treatment.

Importance of exercise during chemotherapy

As retrospective research, conducted by Wonders et al.,[25] has demonstrated, engaging in physical exercise during chemotherapy treatment can be influential in adhering to the

scheduled dose and timing of chemotherapy. Their analysis found that in a sample of 184 patients undergoing treatment for advanced-stage cancers, those who participated in a structured exercise program were better able to maintain their chemotherapy schedule and dose. Specifically, the study showed that while there was a range of 12% to 83.9% of patients who missed at least one dose of a myelosuppressive agent, overall, patients with advanced cancer who maintained an exercise adherence rate above 84.3% experienced fewer chemotherapy dose delays and reductions. This was a significant finding when compared to disruption frequencies in the sedentary population.

Furthermore, the study revealed that less than half (50.8%) of the patients received less than 85% of the relative total dose intensity, which is the designated threshold for a clinically meaningful reduction in treatment. This is important because maintaining a high RDI is correlated with improved patient outcomes, such as overall survival and disease-free survival rates.

The exercise protocol in the study was comprehensive, incorporating cardiovascular, resistance, and flexibility exercises, under the supervision of a certified exercise oncology trainer. These exercise sessions were tailored to each patient's ability and were modified progressively, showing a personalized approach to the integration of exercise in the treatment plan.

Moreover, the regimen included at least 12 weeks of prescribed individualized exercise in accordance with the American College of Sports Medicine guidelines, and adjustments were made for each patient based on factors such as immune function and proximity to the cancer center.

In summary, this research by Wonders and colleagues suggests that exercise may be a valuable intervention to help cancer patients manage their chemotherapy treatments more effectively. It underscores the potential benefits of exercise in maintaining dose intensity, potentially leading to better treatment outcomes. Exercise appears to be a supportive measure that could be advocated for more broadly among patients receiving chemotherapy for advanced cancers.

Recommendations for healthcare providers

Increasing treatment adherence in patients undergoing medical therapies, such as chemotherapy for leukemia or lymphoma, involves a multifaceted approach that addresses both the logistical and psychological aspects of treatment.

Ensure that patients fully understand their diagnosis, treatment plan, potential side effects, and the significance of sticking to the prescribed regimen. Empowering patients with knowledge enables them to take an active role in their own care.

Identify and eliminate barriers to care, including transportation issues, financial constraints, and language differences. Introduce support services such as transport assistance, financial counseling or interpreter services.

Proactively manage side effects through pre-emptive medication, lifestyle recommendations and alternative support such as acupuncture or massage therapy to make treatments more tolerable.[26]

Offer counseling, support groups and mental health services to help patients cope with the emotional and psychological effects of their illness and treatment, providing psychosocial support.[27][28]

Utilize technology such as smartphone apps, text messaging or automated calls to remind patients about their medication schedule.

Foster strong, trust-based relationships between patients and healthcare providers to ensure open lines of communication. This will help patients feel more comfortable discussing challenges with adherence.

Encourage a strong support system involving family and friends in the patient’s treatment plan to provide emotional support, assistance with medication administration, and practical help during challenging times.

Schedule regular follow-up appointments to monitor progress, reinforce the importance of adherence, and adjust treatment as necessary.

Recognize that different patients have different needs and tailor adherence strategies accordingly. Personalize interventions based on the patient's lifestyle, beliefs and preferences.

Engage in shared decision-making, allowing patients to have a voice in their treatment choices, which can increase their commitment to the selected treatment regimen.[29]

Provide positive reinforcement for adherence through praise during appointments or other reward-based systems to motivate patients.

Have a readily accessible healthcare team that patients can contact with questions or issues related to their treatment.

Offer patients written instructions and educational materials about their medications and treatment to refer back to as needed.

Optimal chemotherapy protocols are essential to increase treatment efficacy and patient survival rates while minimizing harmful side effects. Personalized regimens ensure that patients receive precisely calibrated doses, enhancing their quality of life during and after treatment. By reducing toxicity, optimal protocols can improve patient compliance, leading to better overall treatment success. Advances in chemotherapy protocols can also lower healthcare costs by diminishing the need for supportive interventions and hospitalizations. Ultimately, the development of more refined chemotherapy treatments is key to transforming cancer care into a more targeted and patient-centered practice.

Designing an optimal chemotherapy protocol requires detailed patient-specific data, including the genetic and molecular characteristics of malignancy and the individual health status of the patient.[30] The selection of chemotherapy agents and the establishment of safe and effective dosage ranges for each drug based on clinical data are also crucial. An understanding of the drugs' pharmacodynamics is necessary to inform dosing and timing, as well as pharmacokinetics modeling to fine-tune drug concentration profiles within the bone marrow and other tissues.

Determining the optimal dose of each chemotherapy agent is essential to maximize efficacy and minimize toxicity. Setting the infusion durations and intervals for each drug ensures the desired drug exposure is achieved and the creation of a treatment timetable is important to specify when each chemotherapy cycle will be delivered.[31] It is critical that the protocol maintains the total number of normal cells above a certain level throughout the treatment to allow for bone marrow recovery.

Employing optimization algorithms that integrate all the above factors is required to propose an optimal treatment schedule. This involves thorough health assessment, including disease staging and patient-specific factors, as well as computational simulations that incorporate pharmacodynamics and pharmacokinetics models to predict treatment outcomes. The optimized protocol may need to be adjusted based on simulation results and individual patient responses in a continuous feedback loop and validated through controlled clinical trials. Continuous monitoring and adjustment of the patient's response and side effects during the treatment are necessary for potential protocol adjustments. A multidisciplinary approach is needed involving oncologists, pharmacologists, mathematicians and computational biologists to develop and refine the protocol.

The goal is to effectively minimize the cancerous cell population while maintaining the number of normal cells above a defined limit to ensure patient safety and improve therapeutic outcomes.

Conclusion

In conclusion, this in-depth exploration highlights the multifaceted nature of combatting leukemia and lymphoma—two prevalent and impactful forms of cancer. The detailed analysis of their epidemiology reveals the critical importance of understanding how factors such as age, genetic predispositions, and lifestyle contribute to the risk and progression of these diseases. This knowledge is invaluable for both the development of targeted prevention measures and the identification of populations that may benefit from early detection strategies.

Furthermore, the discussion on treatment adherence underscores the necessity of comprehensive patient support throughout the chemotherapy process. The role of healthcare providers in facilitating adherence through education, management of side effects and the reduction of barriers cannot be overstated. Their dedication to improving the patient experience has the potential to significantly enhance treatment outcomes.

The emphasis on the need for more optimal chemotherapy protocols acts as a clarion call for continued innovation in cancer treatment. Personalized medicine stands at the forefront of this endeavor, representing a paradigm shift towards tailored therapies that account for the intricate biological variability of both the cancer and the patient. This level of customization promises to not only improve survival rates but also to preserve the quality of life for those undergoing treatment.

Moreover, these advancements in treatment and patient care are set against the backdrop of a rapidly evolving medical landscape. The integration of cutting-edge research, clinical expertise and patient-centered care is critical. The combined effort of oncologists, researchers, and multidisciplinary teams is essential to refine current treatment options, develop new therapeutic strategies and ultimately, move closer to the goal of effective and compassionate care for all affected by leukemia and lymphoma.

In essence, the collective efforts encapsulated in this discussion provide a beacon of hope for patients, caregivers and healthcare professionals alike. It is through such diligent, informed and patient-focused approaches that the fight against cancer will progress towards more favorable and life-affirming outcomes. As the scientific community continues to push the boundaries of knowledge, the anticipation of a future where cancer is no longer a dreaded prognosis grows ever brighter.

Disclosure

Author's contribution

Conceptualization: Bartłomiej Szymański; Methodology: Andrzej Czajka; Software: Michał Łepik ; Check: Kacper Reguła and Zofia Uszok; Formal analysis: Joanna Wojtania and Bartłomiej Szymański; Investigation: Krzysztof Rosiak, and Bartłomej Szymański; Resources: Zofia Uszok; Data curation: Szymon Piaszczyński - rough preparation: Kacper Płeska and Kacper Reguła; Writing - review and editing: Michał Łepik and Kamil Waloch; Supervision: Joanna Wojtania; Project administration: Bartłomiej Szymański and Kacper Płeska; Receiving funding - no specific funding.

All authors have read and agreed with the published version of the manuscript.

Financing statement

This research received no external funding.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Not applicable.

Conflict of interest

The authors deny any conflict of interest

References

[1] M. Burns et al.. "Identification of prognostic factors in childhood T-cell acute lymphoblastic leukemia: Results from DFCI ALL Consortium Protocols 05-001 and 11-001". Pediatric Blood & Cancer. vol. 68. no. 1. Oct. 2020. https://doi.org/10.1002/pbc.28719.

[2] P. A. Thompson, H. M. Kantarjian and J. E. Cortés. "Diagnosis and Treatment of Chronic Myeloid Leukemia in 2015". SYMPOSIUM ON NEOPLASTIC HEMATOLOGY AND MEDICAL ONCOLOGY. vol. 90. no. 10. pp. 1440-1454. Oct. 2015. 10.1016/j.mayocp.2015.08.010.

[3] R. L. Siegel, K. D. Miller, N. S. Wagle and A. Jemal. "Cancer statistics, 2023". CA: A Cancer Journal for Clinicians. vol. 73. no. 3. pp. 233-254. Mar. 2023. https://doi.org/10.3322/caac.21772.

[4] A. Bonaventure et al.. "Worldwide comparison of survival from childhood leukaemia for 1995–2009, by subtype, age, and sex (CONCORD-2): a population-based study of individual data for 89 828 children from 198 registries in 53 countries". The lancet. Haematology. vol. 4. no. 5. pp. 202-217. Apr. 2017. https://doi.org/10.1016/S2352-3026(17)30052-2.

[5] T. Terwilliger and M. Abdul-Hay. "Acute lymphoblastic leukemia: a comprehensive review and 2017 update". Blood cancer journal. vol. 7. no. 6. pp. 577-577. Jun. 2017. https://doi.org/10.1038/bcj.2017.53.

[6] M. Belson, B. Kingsley and A. K. Holmes. "Risk Factors for Acute Leukemia in Children: A Review". Environmental health perspectives. vol. 115. no. 1. pp. 138-145. Jan. 2007. https://doi.org/10.1289/ehp.9023.

[7] "BCR-ABL1 in leukemia: Disguise master outplays riding shotgu... : Journal of Cancer Research and Therapeutics". Journal of Cancer Research and Therapeutics. vol. 9. no. 1. pp. 610. Nov. 2013. 10.4103/0973-1482.110339.

[8] M. Du et al.. "The Global Burden of Leukemia and Its Attributable Factors in 204 Countries and Territories: Findings from the Global Burden of Disease 2019 Study and Projections to 2030". Journal of Oncology. vol. 2022. pp. 1-14. Apr. 2022. 10.1155/2022/1612702.

[9] S. M. Ansell. "Hodgkin lymphoma: 2018 update on diagnosis, risk-stratification, and management". American Journal of Hematology. vol. 93. no. 5. pp. 704-715. Apr. 2018. 10.1002/ajh.25071.

[10] J. Kuruvilla. "Standard therapy of advanced Hodgkin lymphoma". American Society of Hematology. vol. 2009. no. 1. pp. 497-506. Jan. 2009. 10.1182/asheducation-2009.1.497.

[11] K. C. Thandra, A. Barsouk, K. Saginala, S. Padala, A. Barsouk and P. Rawla. "Epidemiology of Non-Hodgkin's Lymphoma". medical sciences. vol. 9. no. 5. Jan. 2021. https://doi.org/10.3390/medsci9010005.

[12] P. Boffetta. "I. Epidemiology of adult non-Hodgkin lymphoma". EDUCATIONAL BOOK. vol. 22. no. 4. pp. 27-31. Jun. 2011.

[13] M. Al-Hamadani, T. M. Habermann, J. R. Cerhan, W. R. Macon, M. J. Maurer and R. S. Go. "Non-Hodgkin lymphoma subtype distribution,geodemographic patterns, and survival in the US: A longitudinal analysis of the National Cancer DataBase from 1998 to 2011". American Journal of Hematology. vol. 90. no. 9. pp. 790-795. Jun. 2015.

[14] A. Caley and R. J. Frcp. "The principles of cancer treatment by chemotherapy". Surgery. vol. 30. no. 4. pp. 186-190. Apr. 2012.

[15] J. M. Goldman. "Prospects for cure in leukaemia.". Journal of Clinical Pathology. vol. 40. no. 9. pp. 985-994. Sep. 1987. 10.1136/jcp.40.9.985.

[16] V. W. Ing. "The Etiology and Management of Leukopenia". Can Fam Physician. vol. 30. pp. 1835–1839. Sep. 1984.

[17] P. A. Brown. "Treatment of infant leukemias: challenge and promise". Hematology Am Soc Hematol Educ Program. vol. 2013. no. 1. pp. 596-600. Dec. 2013. 10.1182/asheducation-2013.1.596.

[18] G. H. Lyman, E. Abella and R. Pettengell. "Risk factors for febrile neutropenia among patients with cancer receiving chemotherapy: A systematic review.". Critical Reviews in Oncology/Hematology. vol. 90. no. 3. pp. 190-199. Jun. 2014.

[19] J. Kwak, J. Halpern and R. Olshen. "Prognostic significance of actual dose intensity in diffuse large-cell lymphoma: results of a tree-structured survival analysis.". Journal of Clinical Oncology. vol. 8. no. 6. pp. 963-977. Jun. 1990.
[20] R. Epelbaum, N. Haim and M. Ben-Shahar. "Dose-intensity analysis for CHOP chemotherapy in diffuse aggressive large cell lymphom". Israel Journal of Medical Sciences. vol. 24. no. 9. pp. 533-538. Sep. 1988.
[21] G. H. Lyman, J. Crawford, D. Tomita, S. Whittaker and D. C. Dale. "Changing patterns of chemotherapy relative dose intensity and supportive care for aggressive B-cell non-Hodgkin lymphoma". Leukemia & Lymphoma. vol. 57. no. 2. pp. 283-290. Jul. 2015. https://doi.org/10.3109/10428194.2015.1045894.
[22] A. Puła, M. Zdunek, K. Michalczyk, M. Cichosz and W. Młynarski. "Chemotherapy delays in children with acute lymphoblastic leukemia might influence the outcome of treatment". Acta Haematologica Polonica. vol. 53. no. 2. pp. 141-148. Apr. 2022. 10.5603/ahp.a2022.0007.
[23] E. Bowhay-Carnes, C. Fountzilas, M. J. Martinez, B. Konkel, B. Stormes and A. B. Karnad. "Chemotherapy Relative Dose Intensity and Therapy Efficacy in Hodgkin and Non-Hodgkin Lymphoma: The Effect of Dose Reductions and Delays on Cure". blood. vol. 126. no. 23. pp. 5092. Dec. 2015.
[24] G. Rodrigues and M. Sanatani. "Age and comorbidity considerations related to radiotherapy and chemotherapy administration.". Seminars in Radiation Oncology. vol. 22. no. 4. pp. 277-283. Oct. 2012.

[25] Wonders KY, Schmitz KH, Harness J. Dose Delays, Dose Reductions, and Relative Total Dose Intensity in Patients With Advanced Cancer Who Exercised During Neoadjuvant Chemotherapy Treatment. Integrative Cancer Therapies. Vol. 22. April 19, 2023. https://doi.org/10.1177/15347354231168368
[26] T. Bao, J. Hopkins and S. Kimmel. "Use of acupuncture in the control of chemotherapy-induced nausea and vomiting.". Journal of the National Comprehensive Cancer Network. vol. 7. no. 5. pp. 606-612. May. 2009.
[27] L. E. Carlson and B. D. Bultz. "Benefits of psychosocial oncology care: Improved quality of life and medical cost offset". Health and Quality of Life Outcomes. vol. 1. no. 8. Jan. 2003.

[28] D. B. Mitschke. "Cancer in the Family: Review of the Psychosocial Perspectives of Patients and Family Members". Journal of Family Social Work. vol. 11. no. 2. pp. 166-184 . Jul. 2008. https://doi.org/10.1080/10522150802175159.

[29] M. C. Politi, J. L. Studts and J. Hayslip. "Shared Decision Making in Oncology Practice: What Do Oncologists Need to Know?". The oncologist. vol. 17. no. 1. pp. 91-100. Jan. 2012. 10.1634/theoncologist.2011-0261.

[30] E. Pefani, N. Panoskaltsis, A. Mantalaris, M. C. Georgiadis and E. N. Pistikopoulos. "Design of optimal patient-specific chemotherapy protocols for the treatment of acute myeloid leukemia (AML)". Computers & Chemical Engineering. vol. 57. pp. 187-195. Oct. 2013. https://doi.org/10.1016/j.compchemeng.2013.02.003.

[31] E. Frei and G. P. Canellos. "Dose: A critical factor in cancer chemotherapy". The American Journal of Medicine. vol. 69. no. 4. pp. 585-594. Oct. 1980. 10.1016/0002-9343(80)90472-6.