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INFORMATION

For Readers
For Authors
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IN VITRO ANTI-BACTERIAL SCREENING OF DRYNARIYA QUERCIFOLIA

ASHNA T, LINS MARY JOY, SIYARA ANTONY, SINDU T J, SHEEBA MOL P, SHIJI T S, SOUMYA K GEORGE

Pages 120-123

VIEW PDF

CASE REPORT(S)

GUILLAIN-BARRE SYNDROME: A PAEDIATRIC CASE SCENARIO IN A TERTIARY CARE HOSPITAL AT SOUTHERN INDIA

NEVIN JOSEPH, ALFIN BABY, ELDHOSE ELIAS GEORGE, GOPIKRISHNAN T.S, MERRIN JOSEPH

Pages 101-104

VIEW PDF

Research Article

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TOXICITY PROFILE OF CHEMOTHERAPY REGIMENS FOR MULTIPLE MYELOMA PATIENTS USING CTCAE CRITERIA

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Abstract

Background: Multiple myeloma (MM) is a haematological malignancy of B-cells of plasma cells. The increasing incidence of MM and because of the scarcity of Indian studies on this topic, a detailed study regarding the toxicity profile of chemotherapy regimens for multiple myeloma patients using CTCAE criteria is necessary. Aim: The aim of the study is to investigate the toxicity profile of various chemotherapy regimens in MM patients, specifically using the CTCAE criteria. Methodology: The study is retrospective and clinically based, focusing on MM patients who received different chemotherapy regimens (CyBorD, VD, VRD, TD, and RD) at the Caritas Cancer Institute in Kottayam between 2015 and 2019. Patients meeting specific inclusion and exclusion criteria were selected. Toxicity profiles were analyzed at two time points: after 4 cycles of treatment (4 months) and at the end of therapy. Results: The study involved 87 patients with a mean age of 64 ± 11.8years. The majority of patients (83.9%) had MM for less than 2 years. A total of 575 adverse events were reported and categorized based on the CTCAE criteria: 43.5% were Grade 1 (mild), 34.8% were Grade 2 (moderate), 19.1% were Grade 3 (severe), and 2.6% were Grade 4 (life-threatening). The most commonly reported toxicities included anaemia, thrombocytopenia, renal failure, and peripheral neuropathy Conclusion: The study's findings suggest that while toxicities were common among MM patients receiving chemotherapy, the majority were of Grade 1 (mild) severity. Very few cases reached Grade 4, which indicates life-threatening consequences. This information can help healthcare professionals and patients make informed decisions regarding the choice of chemotherapy regimens for MM treatment.

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Introduction

Multiple myeloma as a condition characterized by the accumulation of malignant plasma cells in the bone marrow, which can lead to bone destruction and lesions. The exact cause of MM is not well-established, but it is thought to be influenced by genetic, environmental, and occupational factors [1-5]. Staging is important to determine the extent and location of malignant plasma cells in the body. Various staging systems, such as the Durie-Salmon system and the International Staging System (ISS), are used to assess the severity of the disease. The primary goals of treating MM include achieving a deep and long-lasting clinical response, controlling the growth and spread of malignant cells, reducing complications associated with MM, and improving the overall quality of life for patients. The primary goals of treating MM include achieving a deep and long-lasting clinical response, controlling the growth and spread of malignant cells, reducing complications associated with MM, and improving the overall quality of life for patients. The importance of your study by pointing out that there have been no recent studies on the toxicity profile of MM patients in a clinical care setting in Kerala. This underscores the need for research in this specific region and context. List some of the commonly used drugs in MM treatment, including alkylating agents, proteasome inhibitors, angiogenesis inhibitors, immunomodulators, histone deacetylase inhibitors, and monoclonal antibodies. These drugs are used in various combinations for MM therapy. Main aim of your study, which is to investigate the toxicity profile of chemotherapy regimens for MM patients, using the CTCAE criteria. This will help provide valuable information on the safety and side effects of these treatments.

Materials and methods

This retrospective cohort study involved the comparison of various chemotherapeutic regimens employed in the management of multiple myeloma and an analysis of their respective toxicity profiles. The study spanned a period of 11 months, although data collection was limited to a 5-month duration due to the impact of the Covid-19 pandemic and its associated consequences.

The research was conducted within the Oncology department at Caritas Cancer Institute, Kottayam, affiliated with Caritas Hospital—a tertiary care centre accredited by the National Accreditation Board for Hospitals (NABH). Caritas Hospital boasts specialized institution departments, including Caritas Heart Institute and Caritas Cancer Institute, and offers a bed capacity exceeding 600. The hospital is well-equipped with 10 intensive care units, 18 operating theatres, and various other specialized departments.

Study participants included patients with multiple myeloma who had sought consultation at Caritas Cancer Institute of Caritas Hospital between 2015 and 2019. These patients were selected based on their satisfaction of the predefined inclusion and exclusion criteria.

Inclusion criteria: The study included multiple myeloma patients who had completed specific treatment regimens and had a follow-up period of at least 6 months. The treatment regimens considered were Cyclophosphamide – Bortezomib - Dexamethasone (CyBorD), Thalidomide – Dexamethasone (TD), Bortezomib – Lenalidomide - Dexamethasone (VRD), Lenalidomide - Dexamethasone (RD), and Bortezomib – Dexamethasone (VD).

Exclusion criteria: Patients with other types of cancers, myeloma, pregnancy, different treatment regimens, and those in palliative care were excluded from the study population.

The study encompassed five arms corresponding to patients treated with the different regimens: CyBorD, VD, VRD, RD, and TD. While over 150 multiple myeloma patients consulted Caritas Cancer Institute between 2015 and 2019, only 87 of them were included in the study due to the disruptive impact of the COVID-19 outbreak.

Patient-specific data were collected from their respective case files within the Medical Records Department (MRD). The collected information encompassed the patient's chief complaint at the time of diagnosis, stage and date of diagnosis, past medical and medication history, details of the treatment cycle, any modifications made to the treatment, and the toxicity profile associated with each treatment regimen. The study also documented the effects of treatment regimens on clinical manifestations and laboratory parameters. The toxicity profile was assessed after 4 cycles of the treatment regimens (at the 4-month mark) and upon completion of the therapy.

Toxicity Criteria:Toxicities were graded in accordance with the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5[6]. : Grade 1: Mild - Asymptomatic or mild symptoms, requiring only clinical observation with no intervention indicated. Grade 2: Moderate - Involving minimal or local intervention, possibly limiting activities of daily living, and necessitating appropriate instrumental activities of daily living (ADL).Grade 3: Severe or medically significant but not immediately life-threatening; may require hospitalization or extended hospital stay, and may interfere with self-care ADL. Grade 4: Life-threatening consequences, necessitating urgent intervention. Grade 5: Death related to adverse events.

Results and discussion

The aim of the study was to analyse toxicity profile of multiple myeloma patients treated with different therapeutic regimens. The study was conducted in the Cancer Care Institute of a tertiary care hospital among 87 multiple myeloma patients. The mean age years of the patients were found to be 64 ± 11.8. Toxicities were graded as per the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0[19]. We could find that all the 87 patients enrolled in the study had drug related adverse effects course of therapy. A total of 575 adverse events were reported in which 250 (43.50%) events observed was Grade 1 toxicities which had mild symptoms and toxicities, 200 (34.80%) events were Grade 2 moderate toxicities, 119 (19.10%) events observed was Grade 3 Severe toxicities and about 15 (2.6016%) events were Grade 4 life-threatening consequences. None of them died due to serious and life- threatening adverse effects. The most commonly reported Grade 1 Grade 2 and Grade 3 toxicities were anaemia, hypocalcaemia, leucopoenia, neutropenia, thrombocytopenia, renal failure, peripheral neuropathy, venous thromboembolism (VT). Grade 4 renal toxicities and anaemia were seen in the MM patients. Lofti Benboubker *et al,* demonstrated that grade 3 or 4 adverse events were somewhat less frequent with mine RD (tenalidomide- dexamethasone) regimen than with MPT [7]. A systematic reviews les revealed that grade 3 or 4 adverse events are most frequent in patients with Thalidomide monotherapy [8]. The percentage of toxic events in each grades were summarised in figure1.

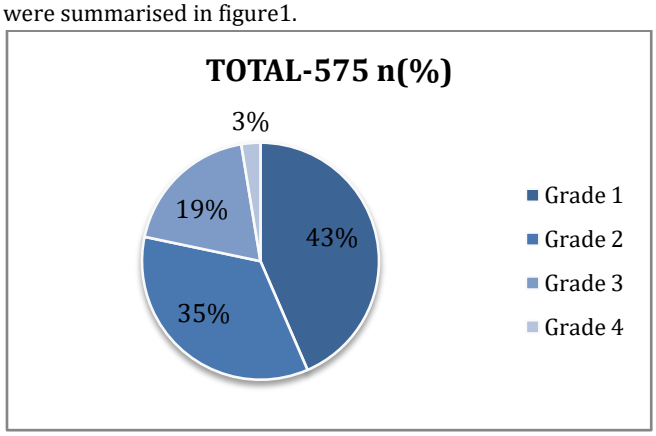

Fig. 1 Gradings of toxicities reported according to CTCAE version 5

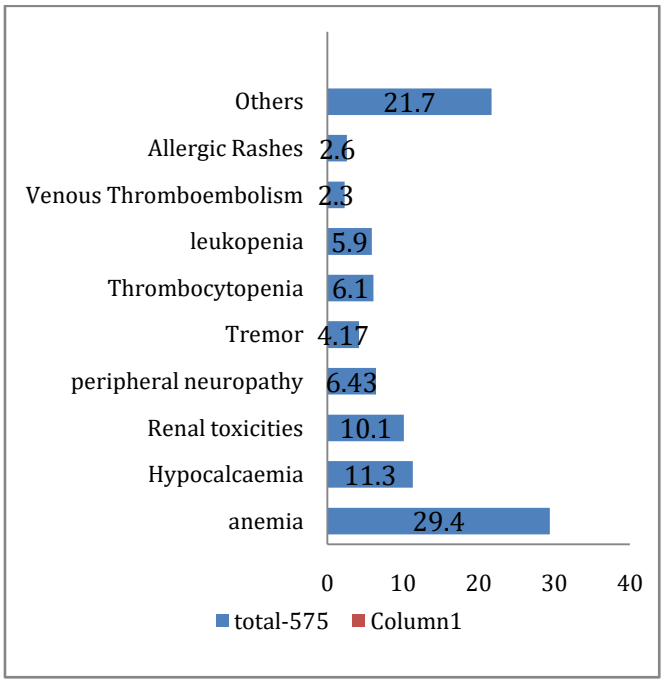

Fig.2 Toxicities Reported

It was found that anaemia was the most common and significant. Similarly, multiple studies have also proven that anaemia rates were higher for patients with MM [9, 10]. In the findings of European Cancer Anaemia Survey, Gunnar Birgegard et al, showed that the highest frequency of anaemia was observed in patients with multiple myeloma (85.3%) [9].In our study about 29.40% anaemia, 11.30% of hypocalcaemia and 10.10% of renal toxicities were reported among the patients who received VD. RD. TD, VRD and CyBord. Thrombocytopenia and Leukopenia was found to be 6.10% and 5.90% respectively. About 6.43% of peripheral neuropathy and 4.17% of tremor was shown by the patients who had RD, VD and TD as their treatment regimens. 2.30% of venous thromboembolism (VT) was found in the patients who had CAD or CVA history and received RD. 2.30% showed allergic rashes to RD. Moreover, mild symptoms like fever, cough with sputum, headache, chills. Diarrhoea, vomiting, viral infections like dengue, herpes infection, viral fever, oral candidiasis, hypoglycaemia, hyperglycaemia, hypoalbuminemia. erythematous plaque, throat erythematous, giddiness, gait unsteadiness, fatty liver, pedal oedema, recurrent UTI, hoarseness, facial puffiness etc. were summarised as others (about 21.70%) in the figure 2.Studies regarding the toxicity management of multiple myeloma patients by Tiffany also reported that myeloma patients have a 7-fold increased risk for bacterial infections and a 10-fold risk for viral infections. He also pointed out that fatigue, gastrointestinal problems, thrombocytopenia, neutropenia, peripheral neuropathy and rashes can be the issues on patients taking several immunomodulatory drugs [11].

Conclusion

The aim of the present study was to analyse the toxicity profile of MM patients treated with different therapeutic regimens. The most commonly reported Grade 1 Grade 2 and Grade 3 toxicities were anaemia, hypocalcaemia, leukopenia, neutropenia, thrombocytopenia, renal failure, peripheral neuropathy, venous thromboembolism. Grade 4 renal toxicities and anaemia were seen in some of the MM patients. The study concluded that even though toxicities are common for patients receiving chemotherapy majority were grade 1(mild) toxicities. And very few were Grade 4 toxicity.

Acknowledgement

Nill

Conflict of Interest

The authors declare that there is no conflict of interest for this study

Author Contribution

All authors have contributed equally.

Informed Consent

Not required

Ethical Statement

Not required

Reference

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