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Original Article

Clinical Outcomes of Patients with Multiple Myeloma Presenting with Renal Failure

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Abstract

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Aims and Objective This article studies the clinical outcome of patients with multiple myeloma who have renal failure at presentation.

Methodology Patients with multiple myeloma presenting with serum creatinine of more than or equal to 2 mg/dL from outpatient department at Sri Ram Cancer Centre, Mahatma Gandhi Medical College & Hospital, Jaipur, Rajasthan, India, were screened for baseline serum creatinine and estimated glomerular filtration rate (eGFR). Assessment was done at completion of 6 months from diagnosis—patients' clinical condition, renal response (serum creatinine and eGFR), and disease response as per the International Myeloma Working Group criteria.

Results Final response assessment was done at a follow-up of 6 months. Half of the patients achieved a renal complete response; the highest being in the lenalidomide group (83.3%). Patients with eGFR < 15 mL/min/m^2 at presentation fared poorly versus those with eGFR > 15 mL/min/m^2. Patients who were dialysis-dependent at baseline had poorer renal responses as compared with those who were dialysis-independent. Out of six patients who were initially dialysis-dependent, four (66.6%) became dialysis-independent after treatment.

Keywords

- creatinine
- dialysis
- light chain
- multiple myeloma
- renal failure

Introduction

Multiple myeloma is characterized by the neoplastic proliferation of clonal plasma cells, which produce excess monoclonal immunoglobulins, light chains, or both, often resulting in organ damage. It is a disease with a relapsing and remitting course. Renal dysfunction at diagnosis presents a great challenge in management and is a factor leading to inferior outcomes.[1]

Managing patients with multiple myeloma and renal failure requires a multidisciplinary approach involving disease-directed therapy alongside renal replacement therapy in cases of severe renal dysfunction. Bortezomib-based

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regimens are the most commonly used first-line regimes in the treatment of multiple myeloma. Owing to ease of accessibility and renal safety profile, bortezomib remains the cornerstone of management of these patients in India. In this study, we present our experience of bortezomib-based triplet regimes in patients with multiple myeloma presenting with renal dysfunction at baseline.

Methods

The aim of this study was to study the clinical outcome of patients with multiple myeloma with renal failure at presentation who were treated with bortezomib-based triplet therapy. This was a prospective observational study conducted at a tertiary hospital in North India from October 1, 2022 to March 31, 2024. Approval from the institutional ethics committee was obtained prior to starting enrolment. Consecutive patients with newly diagnosed multiple myeloma presenting with serum creatinine of more than or equal to 2 mg/dL were included in the study. Those patients with preexisting chronic kidney disease prior to the diagnosis of multiple myeloma and those who died within 2 weeks of diagnosis were excluded. All patients were treated with bortezomib-based triplet therapy (at the discretion of the treating physician). Response assessment was done at completion of 6 months from diagnosis. The International Myeloma Working Group criteria were followed for diagnosis and response assessment.[2] Only patients who had completed 6 months of follow-up were included in the final analysis. Data collection and analysis were done by Microsoft Excel and SPSS.

Results

Thirty patients were enrolled during the study duration. Baseline demographic, clinical, and risk stratification data are presented in ►Table 1. The median age was 60 years, and the male:female ratio was 2:1. Sixteen patients (53.3%) had baseline estimated glomerular filtration rate (eGFR) less than 15 mL/min/1.73 m^2. Six patients (20%) were dialysis-dependent on presentation. Majority of patients had anemia and lytic bony lesions at diagnosis. Half of the patients were International Staging System (ISS) stage III. All patients received bortezomib (1.3 mg/m^2)- and dexamethasone (40 mg weekly)-based treatment regimens; 21 patients (70%) received cyclophosphamide (300 mg/m^2 weekly), 6 patients (20%) received thalidomide (100 mg once a day), and 3 patients (10%) received lenalidomide (10 mg once a day for 3 out of 4 weeks) as the third agent. Renal response analysis was done every month as per the criteria for renal response to antimyeloma therapy, out of 30 patients 27 patients achieved some kind of renal response, the minimum being a minor response.

The final response assessment was done at a follow-up of 6 months (►Table 2). Half of the patients achieved a renal complete response (CR); the highest being in the lenalidomide group (83.3%). Patients with eGFR < 15 mL/min/m^2 at presentation fared poorly versus those with eGFR > 15 mL/min/m^2 (combined renal CR and partial response [PR] rates 36% vs. 92%). Patients who were dialysis-dependent at baseline had poorer renal responses as compared with those who were dialysis-independent (cumulative renal CR and PR, 32% vs. 80%). Out of six patients who were initially dialysis-dependent, 4 (66.6%) became dialysis-independent after treatment. There were no differences in renal responses among those with difference between involved minus uninvolved serum free light chains (dFLC) greater than or less than 1,000 mg/L at baseline. Renal response as per ISS staging; light chain biochemical response at 6 months were CR (16%), very good PR (VGPR) (26%), PR (23%), stable disease (26%), and progression (9%). At 2 months after the start of treatment, 18 patients (60%) achieved biochemical CR or VGPR; renal CR in this group of patients was 72% as against 16% in those who were not in CR or VGPR at 2 months.

Table 1 Baseline patient characteristics

Baseline patient characteristics	$N = 30$
Age (median/range)	60, 38–78
Male (%)	20 (66.6)
eGFR at presentation (MDRD)	
30–59	4 (13.3%)
15–29	10 (33.3%)
< 15	16 (53.3%)
Dialysis requirement (%)	6 (20)
Anemia (%)	22 (73.3)
BMPC (median/range)	33, 0–79
Hypercalcemia (%)	10 (33.3)
Bony lytic lesions (%)	24 (80)
M-band (median/range)	2.99, 0–5.98
Kappa LC (median/range)	1,047, 9.43–60,600
Lambda LC (median/range)	16.2, 4.17–29,485
Difference in FLC (median/range)	1,031, 5.26–31,115
ISS	
I	3 (10%)
II	12 (40%)
III	15 (50%)
High-risk cytogenetics	

Abbreviations: BMPC, bone marrow plasma-cell percentage; eGFR, estimated glomerular filtration rate; FLC, Serum free light chain ratio; ISS, International Staging System; LC, light chain; MDRD, Modification of Diet in Renal Disease; R-ISS, Revised International Staging System.

Discussion

Renal dysfunction is seen in almost half of all patients with multiple myeloma at presentation.[3] It can be related to the circulating paraprotein or unrelated (hypercalcemia, nonsteroidal anti-inflammatory drug use, dehydration, or infection).[3] Most of the paraprotein-related injury is due to myeloma cast nephropathy, characterized by deposition of a cast consisting of monoclonal free light chain along with Tamm–Horsfall protein in the distal tubules. Other

Table 2 Renal response in Patients

Renal response	Overall	Renal CR	Renal PR	Renal MR
All patients	30 (100%)	15 (50%)	5 (16.6%)	10 (33.3%)
VCd	21	9 (42%)	3 (16%)	9 (42%)
VRd	6	5 (83.3%)	1 (16.7%)	0
VTd	3	1 (33%)	1 (33%)	1 (33%)
Baseline eGFR < 15	16 (53%)	3 (18%)	3 (18%)	10 (74%)
Baseline eGFR > 15	14 (75%)	11 (78%)	2 (14%)	1 (8%)
Dialysis dependent	6 (20%)	1 (16%)	1 (16%)	4 (68%)
Dialysis independent	24 (80%)	15 (64%)	4 (16%)	5 (20%)
DFLC > 1,000	20 (66%)	9 (45)	4 (20%)	7 (35%)
DFLC < 1,000	10 (34%)	5 (50%)	1 (20%)	3 (30%)
≥ VGPR at 2 months	18 (60%)	13 (72%)	4 (22%)	1 (6%)
< VGPR at 2 months	12 (40%)	2 (16%)	7 (49%)	3 (25%)

Abbreviations: CR, complete response; eGFR, estimated glomerular filtration rate; MR, minor response; PR, partial response; VGPR, very good partial response.

pathologies seen are light chain amyloidosis and light chain deposition disease. Renal dysfunction is a poor prognostic marker and is associated with inferior overall survival, particularly if it does not improve with treatment.[4] The presence of dialysis dependence is also an adverse prognostic factor in these patients.[5]

Novel agent-based treatment is favored over conventional chemotherapeutic approaches and that is true even in the setting of renal dysfunction.[6] Bortezomib, cyclophosphamide, thalidomide, and dexamethasone can be used without any dose modifications, while lenalidomide may be used in reduced doses. Plasma exchange, high cutoff dialysis, and urine alkalization have not been observed to offer any conclusive benefit and were not used in any of our patients.

Bortezomib-based regimens are the mainstay of treatment of multiple myeloma with renal impairment.[7] We observed renal CR and PR rates of 50 and 16.6%, respectively, and dialysis independence rate of 66.6% with bortezomib-based triplet therapy. In patients with severe renal dysfunction, bortezomib-based triplets have shown renal CR and PR rates of 35 and 12%, respectively, and dialysis discontinuation rates of 57%.[8] In a study from India, Pandey et al showed renal CR and PR rates of 25 and 40%, respectively, in dialysis-dependent patients treated with bortezomib and dexamethasone doublet.[9]

We observed that severity of renal dysfunction at baseline correlated with poor renal outcomes.[10–14] We also observed that patients who attained a rapid biochemical response fared better. This is consistent with other studies using bortezomib-based regimens. Since renal injury is directly related to the circulating paraprotein, rapid clearance of the same with effective antimyeloma therapy provides the best renal outcomes.

In conclusion, we would like to state that treatment of multiple myeloma with Bortezomib + Dexamethasone-based regimes has shown rapid and significant renal response and has also increased the probability of these patients becoming dialysis-independent, further preserving their quality of life.

Conflict of Interest

None declared.

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