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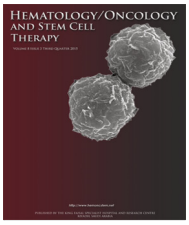

LETTER TO EDITOR

Assessing the safety of autologous stem cell transplant pathway via ambulatory care for patients with multiple myeloma

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Abstract
High-dose chemotherapy (HDT) with autologous stem cell transplantation (ASCT) is the standard of care for eligible multiple myeloma (MM) patients with improved progression-free and overall survival. We reviewed the ambulatory care unit pathway for MM patients who underwent HDT/ASCT in a tertiary hospital to assess safety efficacy and outcomes. We concluded that the ambulatory care model offered for MM patients undergoing HDT/ASCT is a safe alternative pathway and highlighted further improvements.
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Introduction

High-dose chemotherapy (HDT) with autologous stem cell transplantation (ASCT) is the standard of care for eligible multiple myeloma (MM) patients [1] with improved progression-free and overall survival [2].

Our ambulatory care unit (ACU) has been delivering HDT and ASCT for MM patients since 2012. Patients receive conditioning and stem cell return as ambulatory patients with daily clinical review. Direct inpatient admission can be arranged based on clinical indications (e.g., neutropenic fever, symptom control).

Our aim was to review our ambulatory care (AC) pathway for MM patients who underwent HDT/ASCT to assess its safety, efficacy and outcomes.

Methods

We identified patients referred for HDT/ASCT from January to December 2014. We reviewed their clinical records to obtain data including baseline characteristics and peri-transplant issues. We also collected information on disease

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response, complications, readmissions and persisting symptoms up to 1 year post-transplantation.

Results

Baseline characteristics and peri-transplant course

A total of 70 patients were managed in AC for HDT/ASCT in 2014. Five patients with significant renal impairment were excluded after receiving transplant at an alternative institution for renal support. Nine private patients were excluded, and two patients were excluded because they were admitted from the start (one due to new-onset atrial fibrillation and one due to unknown reasons). The remaining 54 patients were included for analysis.

All 54 patients (100%) were admitted to hospital from ACU at a median of 6 days (range, 0—12); commonest indications were neutropenic sepsis and gastrointestinal toxicity (Table 1). Five patients (9%) were admitted very early on day 0/day 1 (D0/D1) of ASCT due to gastrointestinal toxicity. Two patients (4%) necessitated intensive care unit (ITU) referral due to serious cardiorespiratory complications. Patient 1 was admitted to hospital on D0 due to refractory supraventricular tachycardia and necessitated a 24-hour ITU admission for amiodarone and cardiac monitoring. Patient 1 was discharged home on D16. Patient 2 was admitted to hospital on D1 because of progressive respiratory failure secondary to neutropenic sepsis. Patient 2 passed away on D44 due to sepsis. Most patients were discharged home at a median of 17 days (range, 12—32) post-ASCT.

Post-transplant response and complications

Clinical response to transplantation was classified according to the International Myeloma Workshop Consensus Panel [3]. At 3 months post-transplantation, one (2%) remained in complete response, 33 (61%) remained in very good partial response, and 17 (31%) remained in partial response; 52% relapsed post-transplantation. The median progression-free survival is 20.3 months (95% confidence interval, 19.0—21.5) and the median duration to follow-up is 37.4 months (range, 1.5—48.4).

Following discharge, 38 (70%) patients did not require readmissions to the hospital. For those who did, the most common indications were symptom control (nausea, vomiting, diarrhoea and mucositis) (11%) and chest infections (17%). Three (6%) patients were readmitted within a week of discharge; one (2%) for symptom control, one (2%) for non-neutropenic fever and one (2%) for neutropenic sepsis. The most common medical issues reported during outpatient follow-up were symptom control (nausea, vomiting, oral mucositis; 59%), fatigue (52%), musculoskeletal pathologies (44%) such as back pain (26%), neuropathies (31%) and chest infections (28%).

Discussion

Our AC approach for MM patients represents a major change to the previous standard care model [4] at the time of inception. Patients can receive HDT/ASCT on an outpatient basis while staying in a nearby hotel at the hospital's expense [4]. The hotel is located close to the ACU and tertiary hospital. Inpatient admission can be arranged smoothly with a haematology team that is on-site for 24 hours in anticipation of potential medical complications.

Our results suggest that AC is a safe pathway for MM patients undergoing HDT and ASCT. All patients were admitted to hospital for the management of neutropenic sepsis and symptom control issues. This was done in a safe and timely manner, as there were no reported immediate complications. There were two patients (4%) that required ITU admissions: both were admitted early from ACU to the hospital (Patient 1 was admitted on D0, and Patient 2 was admitted on D1). Their morbidities were not attributable to delays that may have occurred due to the AC setting.

The most common peri-transplant issues were symptom control (nausea, vomiting, oral mucositis) and neutropenic sepsis, which is consistent with known toxicity of high-dose melphalan [5]. There were five (9%) very early admissions in ASCT (D0 and D1) due to gastrointestinal toxicity, which highlights a need for vigilant peri-transplant symptom control.

As much as 30% required readmission post-discharge for respiratory infections (17%) and symptom control (11%). One (2%) patient required admission for symptom control within a week of discharge. Post-transplant symptom control could be improved, perhaps with patients counselling and closer monitoring of symptoms during outpatient follow-up, such as nausea and vomiting (59%) and fatigue (52%), with lifestyle advice, exercise programs and diet.

In our clinical experience patients enjoy the greater personal freedom, mobility and time outside of the hospital, although there is no published research on quality of life in the AC pathway. Financial cost savings is one of the biggest advantage, supported by studies which showed that outpatient-based treatment protocols cost significantly less than inpatient care [6,7]. It also allows more appropriate use of limited inpatient resources directed to patients when they require it. Unfortunately, the AC approach is not appropriate for patients with language barrier, poor compliance or those who are unable to advocate for themselves adequately [8].

The AC model offered for HDT/ASCT in MM patients is a safe pathway. Symptom control remains a significant issue up to a year post-transplant, highlighting ongoing patient need in this area. AC could therefore be improved further by addressing early symptom control management. Further work could include longer-term outcomes of AC beyond a year, analysing its cost-effectiveness and collecting anecdotal feedback on patient experience to assess impact on quality of life.

Authors' contributions

All authors contributed to the design of the study, the acquisition, analysis and interpretation of the data. HMY wrote the first draft of the manuscript. KY and DD-S revised the manuscript. All authors approved the final version for publication.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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Table 1 Baseline characteristics.

Total n = 54	Number of patients (% of total/known cases)
Median age (range)	60 (38–70)
Gender:	
Male	39 (72%)
Female	15 (28%)
Isotype:	
IgG	35 (65%)
IgA	12 (22%)
IgD	1 (13%)
Light chain myeloma	6 (2%)
ISS stage:	
1	16 (46%)
2	14 (40%)
3	5 (14%)
Unknown	19 (35%)
Number prior lines therapy before induction and HDT/ASCT	
0	41 (76%)
1	12 (22%)
2	1 (2%)
Melphalan dose (mg/m^2):	
200	53 (98%)
140	1 (2%)
Time to stem cell return:	
24 hours	40 (74%)
48 hours	14 (26%)
Day of hospital admission from AC since D0:	
Median	6 (0–12)
Day of neutrophil engraftment:	
Median	12 (10–25)
Indications for hospital admission from AC:	
Toxicity (nausea, vomiting, diarrhoea, oral mucositis)	17 (31%)
C. difficile diarrhoea	1 (2%)
Neutropenic sepsis	20 (37%)
Non-neutropenic sepsis	3 (6%)
Not specified	12 (22%)
No hospital admission	1 (2%)
Total number of days from admission to AC until discharge	
Median	17.5 (12–32)

AC = ambulatory care; ASCT = autologous stem cell transplantation; HDT = high-dose chemotherapy; Ig = immunoglobulin; ISS = International Staging System.

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