

Hyperbaric Oxygen Decreases Clinical Features associated with Engraftment Syndrome in Multiple Myeloma Patients undergoing Autologous Stem Cell Transplantation

Samuel Weeks¹, Jayesh Menon², Janice Zhao¹, Andrea Baran³, Eric Huselton¹, Jane Liesveld¹, Omar Aljitawi¹

¹Department of Medicine, University of Rochester Medical Center, ²University of Rochester School of Medicine and Dentistry, ³Department of Biostatistics, University of Rochester Medical Center, Rochester NY

Introduction

Engraftment syndrome (ES) is a complication of hematopoietic stem cell transplantation (HSCT) commonly presenting as fever, skin rash, and diarrhea and is associated with the elevation of pro-inflammatory cytokines, including interleukin-6 (IL-6) (Spitzer 2001, Maiolino, Biasoli et al. 2003, Khandelwal, Mellor-Heineke et al. 2016). Hyperbaric oxygen (HBO) can decrease the production of pro-inflammatory cytokines (Benson, Minter et al. 2003, Kudchodkar, Jones et al. 2008) and could therefore theoretically reduce the incidence and or severity of ES.

In this retrospective analysis, we investigate the impact of peri-transplant HBO on the frequency and severity of ES, complications associated with ES and serum concentrations of IL-6 in patients with multiple myeloma receiving autologous transplant.

Methods

Patients were placed in three cohorts including those who did not undergo peri-transplant HBO (n-HBO), received a single treatment of HBO on day 0 of transplant (s-HBO) and received multiple HBO treatments on day 0, +1, and +2 (m-HBO). Patients in the n-HBO and s-HBO cohorts were enrolled in the completed phase II clinical trial (NCT03398200). Patients in the m-HBO cohort were enrolled in the ongoing phase I study (NCT04862676). Grading of oral and GI mucositis was based on the common terminology criteria for adverse events. Enzyme-linked immunosorbent assay (ELISA) for IL-6 was performed from patient plasma samples.

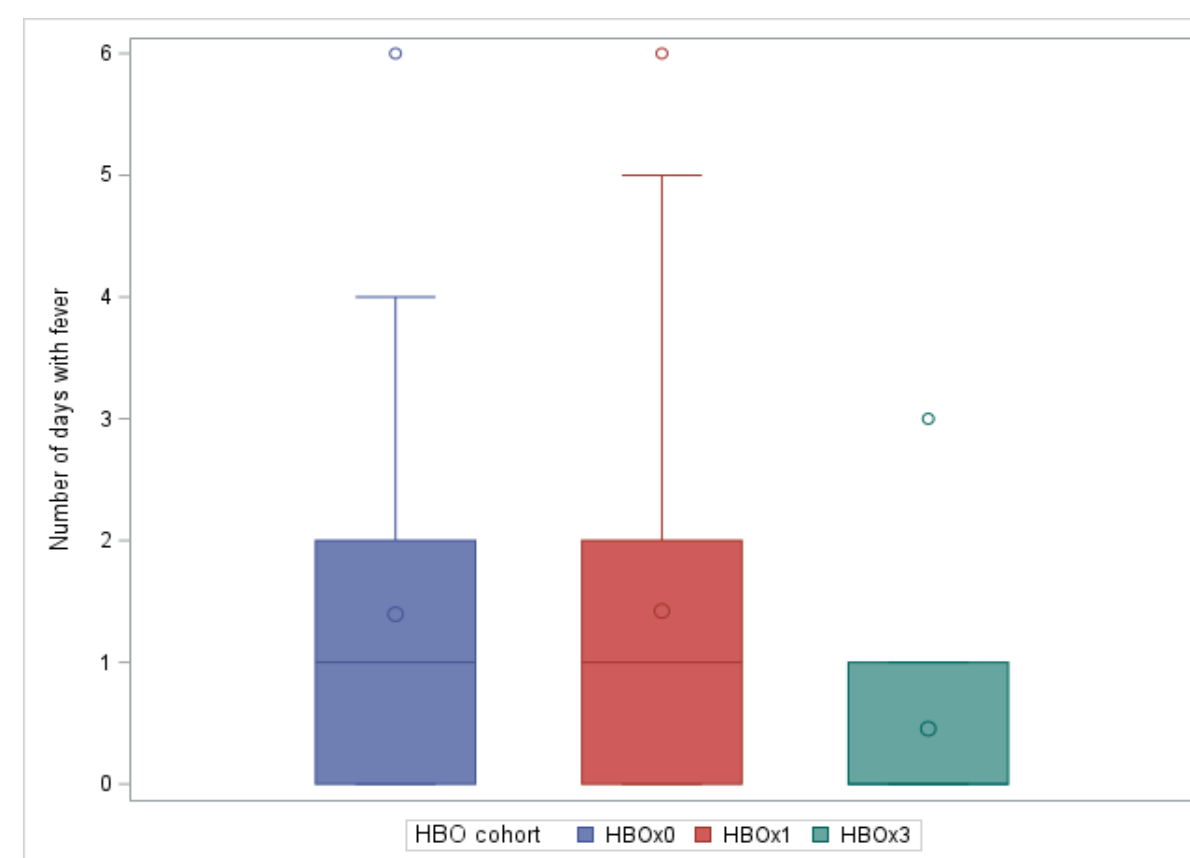


Figure 1: Median number of fever days and IQR by cohort (Kruskal-Wallis p-value=0.04)

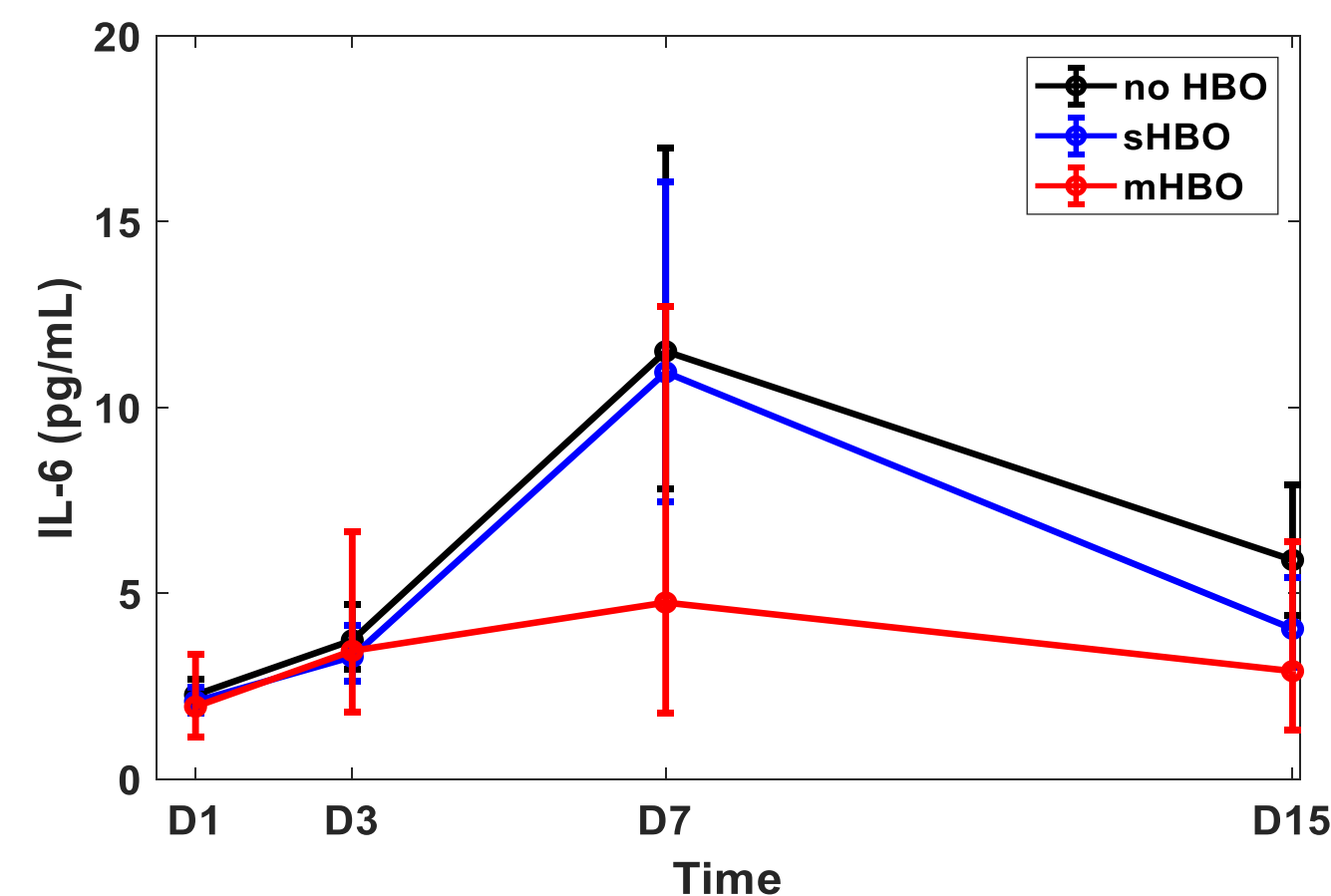


Figure 2: Means and 95% CI of IL-6 concentration by cohort estimated via a linear mixed model (overall treatment arm effect p=0.26)

Results

A total of 87 patients were included in the study. 38 patients were included in the n-HBO and s-HBO cohorts, and 11 were included in the m-HBO cohort. The incidence of ES syndrome, meeting either the Spitzer or Maiolino Criteria, for the n-HBO, s-HBO, and m-HBO cohorts was 27% (95% confidence interval (CI) = 13.8%-44.1%), 21.1% (95% CI = 9.6%-37.3%), and 18.2% (95% CI = 2.3%-51.8%), respectively (Fisher's exact test p=0.77). The median number of fever days for n-HBO, s-HBO, and m-HBO was 1 day (Interquartile range (IQR) 0-2), 1 day (IQR 0-2) and 0 days (IQR 0-1), respectively (Kruskal-Wallis p-value=0.04) (Figure 1). Any grade oral mucositis incidence was 42.4%, 28.6%, and 0% for n-HBO, s-HBO, and m-HBO respectively (Fisher's exact p-value= 0.02). There was only one incidence of grade 3 \geq oral mucositis across cohorts. There was insufficient evidence of a difference in the incidence or duration of GI mucositis between cohorts. Pairwise comparisons using mixed models of IL-6 concentration on day +7 of transplant for m-HBO vs. s-HBO, m-HBO vs. n-HBO, and s-HBO vs. n-HBO resulted in p-values 0.13, 0.11, and 0.85, respectively (figure 2).

Conclusions

In this retrospective study of clinical trial patients, we have shown a significant decrease in clinical features commonly associated with ES, including fever and oral mucositis, in patients receiving m-HBO therapy. Even though the incidence of ES and peak IL-6 was not statistically different with HBO treatment, we observed less incidence of ES and lower IL-6 concentrations with increasing treatments of HBO. This trend may become significant with a larger sample size.