

## Commentary

High-risk leukaemia and a variety of non-malignant haematological illnesses are treated with allogeneic hematopoietic stem cell transplantation (HSCT). Despite improvements in mortality and morbidity over the previous decade, organ toxicity remains a major concern in HSCT, with a no relapse mortality rate of 9 percent to 12 percent at ten years.

Involvement of the liver during the early hazardous phase of HSCT is common. Elevated liver enzymes have been recorded in up to 72 percent of adult patients in the first year following HSCT, [1] while a paediatric research found elevated liver enzymes in roughly one-quarter of children after two years. Previous research from our group has suggested that even modest liver disease in the early post-HSCT period and after a year could be harmful. Despite this, our understanding of the causes of liver involvement in HSCT remains limited; nevertheless, infections and adverse effects of the pre-transplantation conditioning regimen and supportive treatments, as well as acute and chronic graft-versus-host disease, are thought to be multifactorial (GVHD).

Because of transfer of endotoxins originating from the intestinal micro biota, cytotoxic effects of chemotherapy and irradiation on the GI tract are hypothesised to play a crucial role in the aetiology of treatment-related problems in HSCT. Disruption of microbiologically produced products may result in an increase in cytokine concentrations in the portal circulation, exposing the liver to a high load of pro-inflammatory signals and potentially causing further tissue damage and increased all reactivity.

However, potential links between toxic damage to the GI tract and liver involvement, such as sinusoidal obstruction syndrome (SOS), have never been thoroughly studied [2].

The goal of this prospective study was to see if liver disease following HSCT is linked to greater GI toxicity and systemic levels of inflammatory mediators in the early post-transplantation phase. In a group of children and adults, we looked at liver damage and signs of systemic inflammation in the first six months following HSCT. Because citrulline indicates the loss of functioning intestinal epithelial cells and

correlates inversely with clinical and functional scores of GI mucositis, we employed plasma citrulline as a measure of GI toxicity.

From June 2010 to January 2013, we recruited HSCT patients in a prospective research at the national HSCT centre at the Copenhagen University Hospital Rigshospitalet in Denmark. First myeloablative allogeneic stem cell transplantation and age >1 year at the time of transplantation were the inclusion criteria. All of the patients underwent full-intensity conditioning and ceftriaxone and fluconazole as antibiotic prevention. Cyclophosphamide was given to 54 patients as part of their conditioning.

The cohort was previously published, and it consisted of 81 patients out of a total of 154 who had transplantation throughout the study period. Patients who took part in the study had a younger recipient age than those who did not (mean age, 24.3 versus 32.2 years; P.0001). Fewer patients were given complete body irradiation as part of the study [3].

Plasma samples for cytokine and citrulline analyses were taken at predetermined intervals: before the start of the conditioning regimen, on the day of transplantation before graft infusion, on day +7, and on day +21.

Within 2 hours of collection, EDTA-anticoagulated blood and heparinized blood were centrifuged, and plasma was separated and cryopreserved in 5-mL aliquots at 80°C until analysis [4,5].

## References

1. Bearman SI (1995) The syndrome of hepatic veno-occlusive disease after marrow transplantation. *Blood* 3005-3020.
2. Jones RJ (1987)