PB2193 IS HYPERHYDRATION NECESSARY FOR HIGH DOSE MELPHALAN CONDITIONING REGIMEN IN AUTOLOGOUS HAEMATOPOIETIC STEM CELL TRANSPLANTATION?

**Topic:** 22. Stem cell transplantation - Clinical

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**Background:**

Single-agent Melphalan or combined with Bortezomib is often used as a conditioning regimens in autologous haemopoietic stem cell transplantation (HSCT) for multiple myeloma (MM) and primary amyloidosis (AL). In order to prevent nephrotoxicity, Melphalan is often administrated with hyperhydration (HH) consisting of 4-6 Litres (L) 0.9% saline which has a potential fluid overload risk, mainly in elderly patients.

Given the potential morbility of HH, some institutions use a less intensive hydration regimen consisting of 2-3L 0.9% saline the day Melphalan is administrated.

**Aims:**

This study aimed to retrospectively analyze the safety of not using hyperhydration (NHH) in our center.

**Methods:**

This study used a retrospective cohort design, reviewing patients from Guadalajara University Hospital diagnosed with MM or AL who underwent autologous HSCT between January 2017 and December 2021. Cohorts were defined by HH (6L/24h 0.9% saline) or NHH (2L/24h 0.9% saline) the day Melphalan was administrated.

The primary endpoint of this study was the incidence of acute renal impairment, the secondary endpoints were fluid overload and other adverse effects.

Comparisons were assessed using Student t-test or Fisher’s exact test, considering a p-value <0.05 statistically significant.

**Results:**

The sample included 50 patients: 11 with HH (100% MM) and 39 NHH (87.18% MM, 12.82% AL). Patient’s gender (HH 45.45% women; NHH 61.54% women) was similar in both cohorts. Median age in HH cohort was 71, while in NHH it was 61.

The prevalence of kidney disease due to MM at diagnosis was higher in NHH cohort (HH 9.1%, NHH 17.9%; p=0.48) but not statistically significant. Baseline creatinine (HH 0.79, NHH 0.78; p=0.92) and the prevalence of cardiovascular risk factors (HH 63.6%, NHH 66.7%; p=0.31) were comparable.

The incidence of acute renal failure (HH 18.1%, NHH 7.7%; p=0.31) was higher in HH but statistically non-significant, while median creatinine increase from Melphalan administration to day 7 after haemopoietic stem cell infusion was similar in both groups (HH 0.38, NHH 0.18; p=0.08). All patients who developed acute renal failure had a history of chronic kidney disease or a baseline creatinine >1 before HSCT and it was always reversible. Likewise,
all patients developed mild kidney injury (AKIN stage 1) except for one (1/5) from the HH cohort (AKIN stage 3).

Concerning the presence of clinical fluid overload, it was significantly more frequent in the HH cohort (36.6%) in opposition to the NHH cohort (7.7%) (p = 0.02) as expected due to the greater volume administrated, but no patients developed acute pulmonary edema.

Regarding other adverse effects as hepatic toxicity (HH 0%, NHH 17.9%; p=0.13), rash (HH 9.1%, NHH 5.1%; p=0.63) or grade IV mucositis (HH 81.8%, NHH 64.1%; p=0.07), they were similar in both cohorts with no statistically significant difference between both groups.

Neutrophil engraftment was reached at day +10 in HH group and at day +14 in NHH group. This difference is probably due to the elimination of G-CSF from the protocol in the last years in order to avoid engraftment syndrome.

There were limitations in this study such as the small sample size and retrospective analysis.

Image:

| HYPERHYDRATION FOR MELPHALAN CONDITIONING REGIMEN IN AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION |
|------------------------------------------------------------------------------------------------|
| NO HYPERHYDRATION COHORT (NHH) (n=39) | HYPERHYDRATION COHORT (HH) (n=11) |
|---------------------------------------|-----------------------------------|
| **SEX** | | **SEX** | |
| Men | 58.64% (15) | Women | 62.54% (20) |
| Women | 41.36% (14) | Men | 37.46% (7) |
| **DIAGNOSIS** | | **DIAGNOSIS** | |
| Myeloma | 87.18% (34) | Myeloma | 100% (1) |
| Amyloidosis | 12.82% (5) | Amyloidosis | 0% (0) |
| Bortezomib-Melphalan | 2.56% (1) | Bortezomib-Melphalan | 100% (1) |
| Melphalan 200 | 27.44% (10) | Melphalan 200 | 0% (0) |
| Neutrophil >100 | +14 | Neutrophil >500 | +10 |
| Platelet>20,000 | +12 | Platelet>20,000 | +14 |
| **ACUTE KIDNEY FAILURE INCIDENCE** | 7.7% (3) | **ACUTE KIDNEY FAILURE INCIDENCE** | 18.1% (2) |
| **FLUID OVERLOAD INCIDENCE** | 7.7% (3) | **FLUID OVERLOAD INCIDENCE** | 55.4% (4) |

Summary/Conclusion: Hyperhydration did not demonstrate to protect the kidney compared to non-hyperhydration regimes, with a significantly greater incidence of fluid overload. Consequently, HH may not be necessary for melphalan conditioning regimen in autologous haemopoietic stem cell transplantation as our protocol demonstrates an adequate safety profile.