Prevalent vitamin D deficiency and impact of vitamin D on acute GVHD in HCT

Linda DuPuis-Rosen RN, BSN, OCN, Tara Coghlin-Dickson MS, RD, CSSD, Kate Tierney RN, PhD., Laura Johnston MD, David Pickham, RN PhD.
Should we supplement patients with vitamin D during hematopoietic cell transplant (HCT)?

- Vitamin D is an essential mineral with function range from mediating bone hemostasis to immune modulation
- Vitamin D production requires the skin, liver and kidney to convert it to its active form
- HCT patient’s are at increased risk of vitamin D deficiency due to multiple variables such as:
  - use of immunosuppressive medications
  - corticosteroids
  - altered gastrointestinal absorption
  - lack of sun exposure
  - allogeneic myeloablative treatments
INTRODUCTION

• The impact and prevalence of vitamin D deficiency after hematopoietic cell transplant (HCT) is not well known
• Symptoms are vague and subtle such as muscle weakness and pain
• Deficiency of vitamin D can impair bone health and compromise immune status
• Graft Versus Host Disease (GHVD) is a life threatening reaction of donor immune cells against host tissues which can occur as acute and/or chronic after HCT

• Vitamin D deficiency may increase the risk of acute GVHD due to the loss of known immunomodulatory effects
• Questions still remain on the potential buffering of acute GVHD by vitamin D supplementation
Low levels of 25-hydroxyvitamin D before allogeneic hematopoietic SCT correlate with the development of chronic GVHD
Vitamin D Deficiency Predicts Acute Cutaneous Graft-Versus-Host Disease in Reduced-Intensity Allogeneic Hematopoietic Stem Cell Transplantation

- Vitamin D may confer a protective effect against acute skin GVHD via reduction in CCR4 expression
CURRENT RESEARCH GAPs

• Current research shows vitamin D deficiency has been associated with chronic Graft Versus Host Disease (cGHVD), and insufficient vitamin D levels have been shown in patients who have undergone hematopoietic cell transplant (HCT)

• We have limited data on vitamin D deficiency and acute GVHD
Vitamin D deficiency is prevalent in the HCT population

Vitamin D deficiency increases the risk of acute GVHD
METHODS

• Retrospective, pilot study

• Timeline:
  • first quarter- complete data gathering
  • second quarter- finalizing data
  • third quarter- analysis
  • fourth quarter- compile and report results

• Stem Cell Therapeutics Lab provide vitamin D levels from n=50 consecutive, allogeneic myeloablative HCT patients

• Each patient with at least one baseline vitamin D level and levels at +30 days, + 60 days, and +90 post transplant

• Incidences of acute graft vs host disease

• Clinical data was obtained from the BMT registry, EPIC and subjects’ clinical record

• Vitamin D levels were dichotomized at 25ng/ mL
77% of samples (116/150) were below threshold for vitamin D (<25 ng/ml). 74% were vitamin D deficient pre-HCT (20±8 ng/ml). Significantly decreased by day +30 (16±8 ng/ml, \(p = .048\)) and remained constant at day +90 (16±10 ng/ml). Only 6% had normal Vit. D levels at all the 3 time points. None of these patients (3/3) had GVHD.
GVHD was present in 46%. No significant relationship to vitamin D and aGVHD \( (p=.9) \), but all 15 subjects with grade II-IV had vitamin D deficiency (median 12±6 ng/ml, range 5-23ng/ml, \( p=.08 \))
RESULTS OF PILOT STUDY

• Majority pt. samples (77%) were below threshold for vitamin D (<25 ng/ml)
  • Only 3/50 (6%) had normal vitamin D levels at all the 3 time points

• A significant decline in vitamin D levels at day 30 post-HCT
  • 73% had vitamin D deficiency at baseline (20±8 ng/ml)
  • significantly decreasing at 30 days (16±8 ng/ml, \( p=\text{.048} \))
  • remained constant at 90 days (16±10 ng/ml)

• All subjects with acute GVHD (grade II-IV) had vitamin D deficiency
  • All 15 subjects with grade II-IV GVHD at 90 days had vitamin D deficiency (median 12±6 ng/ml, range 5-23ng/ml, \( p=\text{.08} \))

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CONCLUSION

• This study identifies prevalent vitamin D deficiency within this cohort. As a pilot study, we are unable to determine an association with acute GVHD.

• Given our findings as well as other recent research, it compelled our Blood and Marrow Transplant (BMT) program to adopt a standard of care for monitoring and supplementing vitamin D.
IMPLEMENTATION OF VITAMIN D SUPPLEMENTATION

• Systematic check of vitamin D levels on all BMT patients
  • Pre transplant level (within a 7 day range)
  • + 30 days post transplant
  • + 60 days post transplant
  • + 90 days post transplant
  • + 1 year and annually post transplant

• Supplementation of vitamin D to maintain levels => 25 ng/ml
  • < 25 ng/ml supplement weekly 50,000 IU D2 ergocalciferol weekly (prescription) to take with dinner (high fat meal to enhance absorption)
  • > 25 ng/ml supplement with daily 1,000 IU D3 cholecalciferol over the counter (certified product)
COMMUNICATION: BMT VITAMIN D STANDARD OF PRACTICE FOLLOW UP

- Faculty meeting communication and updates
- Inpatient/outpatient inservices (RNs, APPs, Fellows)
- RN Coordinator meetings
- Newsletters
- Inclusion in BMT MD guidelines
- Incorporation into RN/Group message boards in patient charts
- EPIC charting templates (APPs, RNs, RDs, Fellows)
- Communication at multidisciplinary rounds
- Inclusion in pre-transplant letter to referring MD
GOALS FOR MOVING FORWARD

- Increase “compliance” for early and monthly level checking
- Increase “compliance” for supplementation timing and accuracy
- Optimize intake of Vitamin D- starting early pre transplant
  - initiating as soon as possible post level result
  - minimizing missed doses
- Gather new data for a powered study with goal of N=300
- Analyze data
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