Oral microbiome and oral mucositis in autologous hematopoietic stem cell transplantation recipients

Faculty disclosure

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Introduction

• Conditioning for hematopoietic stem cell transplantation (HSCT) frequently leads to oral ulcerative mucositis
• Recently more interest in role of bacteria in disease
• Goal: study the role of oral microbiome in oral mucositis in HSCT recipients

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Materials and methods

• Prospective observational multicenter study
• Autologous HSCT
• Cryotherapy
• Oral ulcerative mucositis (WHO ≥ 2)
• Oral rinse 10 ml (NaCl / PBS)
• Prophylaxis bloodstream infection
  – ciprofloxacin, feneticilline
Flow chart study

Pre-HSCT
- Dental assessment before HSCT

Day 0
- Bedside examinations 3 times per week - until discharge
  - Oral mucositis
  - Salivary flow
  - Oral rinse

Day 100
- Dental assessment
  - Caries
  - Periodontal status
  - Oral infections
  - Salivary flow
  - Oral rinse
Microbiome analysis

- 16S rDNA amplicons were sequenced on the Illumina platform.
- Reads were clustered in oligotypes and classified in taxa.
- Statistics: principal component analysis, PERMANOVA, Shannon diversity Index, LEfSe.

(Figures and tables are not included in the text representation.)
Results

- 50 patients with multiple myeloma
- HSCT, conditioning high dose melphalan
- Age 57.4±7.3 years; 55% males
- 20 patients WHO ≥ 2 (40%)
- 30 patients no ulcerative OM
- 478 oligotypes -> classified in 62 genera
- The most abundant genera:
  - *Streptococcus* (24%)
  - *Prevotella* (20%)
  - *Veillonella* (20%)
No ulcerative mucositis

Lactobacillus
Scardovia

Veillonella
Actinomyces
Prevotella
Leptotrichia
Megasphaera

PERMANOVA: $F=2.84, p=0.0001$

PC1 (16% of variance)

PC2 (9% of variance)

Ulcerative mucositis

Staphylococcus
Scardovia
Enterococcus

Streptococcus
Veillonella
Actinomyces
Gemella

PERMANOVA: $F=2.92, p=0.0001$

PC2 (9% of variance)

PC1 (17% of variance)

PCA: Black – baseline, aqua – days 0-4, fuchsia – 1 week, blue – 2 weeks, green – 100 days
Shannon Diversity Index

Lines connect statistically significant visit pairs (GLM RM test, p<0.001)
Potential biomarkers for oral ulcerative mucositis

**No ulcerative mucositis**
- Streptococcus
- Actinomyces

Aerobes, oral flora
Early colonizers

**Ulcerative mucositis**
- Veillonella
- Enterococcus
- Streptococcus
- Staphylococcus
- Fusobacterium
- Prevotella

Anaerobes, skin flora
disbiosis

LEfSe: linear discriminant analysis effect size
Conclusion

- The oral microbiome shifted and diversity decreased after HSCT, independent of clinical manifestations of oral mucositis
- Shift and decrease in diversity is sooner and more severe in ulcerative mucositis patients
- Certain species present before HSCT were associated with development of oral ulcerative mucositis
- Future studies:
  - alloSCT
  - Fungi
  - Dental status and microbiome
Bray-Curtis similarity index