**Evaluation of peripheral eosinophilia in patients on daptomycin**

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**PURPOSE**

- To determine if daptomycin is associated with peripheral eosinophilia in patients who have received therapy for ≥ 5 days compared to vancomycin

**BACKGROUND**

- Daptomycin is a cyclic lipopeptide antibiotic with a broad spectrum of activity\(^1\)
- It is a popular agent against Methicillin-resistant Staphylococcus aureus (MRSA) and Vancomycin-Resistant Enterococcus (VRE) due to its convenient once daily dosing and safe use in renal dysfunction\(^2\)
- Despite a favorable side effect profile, several cases of daptomycin-induced eosinophilic pneumonia (EP) have been reported\(^3,4,5,6,11,12,13,14\)
- To date, only one case of daptomycin-induced eosinophilia without pulmonary involvement has been reported\(^6\) but the development of peripheral eosinophilia with daptomycin use has never been studied
- If daptomycin-induced eosinophilic pneumonia is preceded by peripheral eosinophilia, it may be an important clinical marker allowing for early termination of daptomycin before the development of eosinophilic pneumonia
- In addition to the potential development of EP, persistently elevated eosinophils can create a pro-inflammatory response and can ultimately lead to permanent tissue damage

**METHODS**

- **Study Design:** Retrospective cohort analysis from June 2013- July 2014
- **Study Eligibility:**
  - Inclusion Criteria: Age ≥ 18 years of age who have received vancomycin or daptomycin for ≥ 5 days
  - Exclusion Criteria: Eosinophilia present prior to antibiotic initiation, asthma, eczema, parasitic disease, B and T Cell lymphoma, solid lung tumors, systemic lupus erythematosus, or rheumatoid arthritis
- **Primary Endpoint:** Incidence of peripheral eosinophilia in patients on daptomycin for ≥ 5 days
- **Secondary Endpoints:**
  - Average dose of daptomycin when eosinophilia present
  - Time to onset of eosinophilia
  - β-lactam exposure
  - Degree of eosinophilia\(^3\)
    - Mild: AEC 351-1499 cells/mm\(^3\)
    - Moderate: AEC 1500-5000 cells/mm\(^3\)
    - Severe: Eosinophilia: AEC > 5000 cells/mm\(^3\)

**OUTCOMES**

| Baseline Characteristics | Daptomycin (n=37) | Vancomycin (n=94) | p-value
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<tbody>
<tr>
<td>Age, yrs. (SD)</td>
<td>54.9 (16.7)</td>
<td>56.36 (17)</td>
<td>0.649</td>
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<td>Gender, n (% male)</td>
<td>27 (73)</td>
<td>52 (55)</td>
<td>0.076</td>
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<td>Race, n (% Caucasian)</td>
<td>35 (94.6)</td>
<td>87 (92.6)</td>
<td>0.51</td>
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<tr>
<td>Weight, kg (SD)</td>
<td>83.9 (26.4)</td>
<td>85.5 (17.8)</td>
<td>0.72</td>
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<td>Initial WBC, cell/mm(^3) (SD)</td>
<td>11.3 (4.6)</td>
<td>13.8 (7.1)</td>
<td>0.011</td>
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<td>Initial eosinophil count, cell/mm(^3) (SD)</td>
<td>88.3 (85.8)</td>
<td>76.84 (85.7)</td>
<td>0.493</td>
</tr>
<tr>
<td>β-lactam exposure, n (%)</td>
<td>23 (62.2)</td>
<td>80 (85.1)</td>
<td>0.004</td>
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**Primary Outcome**

| Development of Eosinophilia, n (%) | Daptomycin (n=37) | Vancomycin (n=94) | p-value | Odds Ratio (95% Confidence)
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<td>17 (45.9)</td>
<td>21 (22.3)</td>
<td>0.007</td>
<td>2.96 (1.32-6.63)</td>
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**Secondary Outcomes**

- **Patients on higher doses of daptomycin were more likely to develop eosinophilia compared to patients on vancomycin (7.01 mg/kg vs. 6.2 mg/kg, p= 0.031)**
- **Time to onset of eosinophilia was not statistically significant, taking 7.2 days in the daptomycin group and 6 days in the vancomycin group (p=0.274)**
- **β-lactam exposure was not found to be a significant confounder in eosinophilia development 0.73 (85% CI 0.29-1.85)**
- **All patients developed mild eosinophilia (AEC of 350-1500 cells/mm\(^3\)), with the exception of one patient who developed moderate eosinophilia (AEC of 2367 cells/mm\(^3\)).**
- **White blood cell (WBC) count did influence the development of eosinophilia, indicating that patients with a higher WBC count were more likely to develop eosinophilia 1.08 (95% CI 1.003-1.17)**
- **A post-hoc analysis revealed that a sample size of 297 (74 patients in daptomycin group and 223 patients in vancomycin group) would have been needed to achieve statistical significance if the AEC threshold was raised to > 500 cells/mm\(^3\)**

**CONCLUSIONS**

- **Patients in the daptomycin group were nearly 3 times more likely to develop a mild peripheral eosinophilia, especially those on higher doses**
- **Since this research commenced less than a year ago, five new case reports of EP linked to daptomycin use have been published and many of these cases were accompanied by peripheral eosinophilia\(^10,11,12,13,14\)**
- **This study does not elucidate whether or not the patients who developed peripheral eosinophilia went on to develop EP; however, there is a clear link between mild eosinophils and daptomycin use**
- **Future studies are necessary to determine if peripheral eosinophilia is a precursor to EP**
- **If peripheral eosinophilia is found to develop prior to EP, it will be important to determine how frequently eosinophil counts will need to be monitored**

**REFERENCES**


**DISCLOSURE**

- None of the authors of this presentation have anything to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.