Inhibition of P. gingivalis-Induced Acute Phase Response in Mice

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Objective: We previously showed that murine infection with the periodontal pathogen Porphyromonas gingivalis (P. gingivalis) induces an increase in serum levels of the murine acute phase protein serum amyloid A (SAA), which is significantly correlated with an increase in aorta atheroma lesion size. The objective of this study was to determine whether antimicrobial therapy with amoxicillin would reduce the hepatic acute phase response in P. gingivalis-infected mice.

Methods: Twenty-seven C57Bl/6J male mice were used with a subcutaneous chamber model of P. gingivalis infection. Mice were divided into three groups and treated with daily injections of either saline intra-chamber (IC), Amoxicillin IC at 20mg/kg, or amoxicillin intra-peritoneal (IP) at 20mg/kg. Injections were given daily two days before and thirty days after live P. gingivalis A7436 challenge. Serum and mouse weight data were collected prior to live P. gingivalis challenge (day -10), and after live P. gingivalis challenge during drug treatment (days +4, +11, and +32). Serum was quantified for SAA by ELISA.

Results: Mean±SD SAA concentration (mg/ml) in each treatment group at different days.

<table>
<thead>
<tr>
<th>Days</th>
<th>-10</th>
<th>4</th>
<th>11</th>
<th>32</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline IC</td>
<td>0.57±0.84</td>
<td>2279.8±2310.5</td>
<td>1688.3±2238.8</td>
<td>85.1±151.1</td>
</tr>
<tr>
<td>Amoxicillin IC</td>
<td>1.90±1.92</td>
<td>6.16±9.27</td>
<td>1.55±1.99</td>
<td>0.55±0.32</td>
</tr>
<tr>
<td>Amoxicillin IP</td>
<td>0.86±0.71</td>
<td>577.0±1004.7</td>
<td>606.4±1290.1</td>
<td>75.5±149.6</td>
</tr>
</tbody>
</table>

P. gingivalis challenge induced a 1000-4000-fold increase in serum levels of SAA at day 4, with a large mouse-to-mouse variability. Using t test to compare the means between groups, values at day 4 and 11 for the amoxicillin IC group were significantly different from the values for the saline group at the same days (P<0.01), while values for the amoxicillin IP group were not significantly different.

Conclusion: Amoxicillin inhibition of the acute phase response induced by P. gingivalis infection in our murine model suggests the potential application of this model to develop new therapeutics for the treatment of both periodontal disease and cardiovascular disease. Supported by NIDCR-DE14459.

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