Use of pepsin detection to identify airways reflux in a range of pulmonary diseases

The diagnostic test Peptest™ detects pepsin in expectorated saliva and is established as a quick and easy measure of the reflux of gastric contents responsible for gastro-oesophageal reflux disease and extra-oesophageal reflux into the laryngopharynx (1, 2). There is evidence that reflux into the airways (lower and upper lungs) is responsible for aetiology or exacerbation of a range of respiratory conditions (3–5).

We hypothesised that detection of pepsin using Peptest™ could provide objective evidence of a contribution of airways reflux in the pathology of a range of pulmonary diseases. In this pilot investigation, Peptest™ was used in patients presenting to the Department of Pneumology and Physiology at a teaching hospital in the Czech Republic. A saliva sample was collected (in citric acid) and applied to a Peptest™ diagnostic test (for Methods see ref (1); www.peptest.co.uk). The lower limit of detection is 16 ng/mL. All samples were tested on site at Charles University and rated as either positive, weak positive or negative.

Our study assessed 352 patients with a range of respiratory/pneumological diseases for the presence of pepsin in a single expectorated saliva sample, as an indicator of reflux. 283 patients (80%) were shown to be pepsin positive (Table 1). There were large groups of patients presenting with bronchial asthma, chronic cough (CC), idiopathic pulmonary fibrosis (IPF), progressive sarcoidosis, exogenic allergic alveolitis, chronic obstructive pulmonary disease (COPD) and a small cohort of cystic fibrosis (CF) patients. There was a high rate of detection of pepsin by Peptest™ in these patients ranging from 74% to 89% (Table 1). The conditions in which we showed with the greatest coexistence of reflux were IPF (89%) and CF (86%; although only n = 7). The data presented in this study were comparable to previous Peptest™ pepsin detection studies which provide additional evidence to the role of pepsin and reflux in these lung diseases.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Peptest Positive (%)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>78%</td>
<td>81 (8)</td>
</tr>
<tr>
<td>CC</td>
<td>87.5%</td>
<td>16 (8)</td>
</tr>
<tr>
<td>COPD</td>
<td>66.7%</td>
<td>12 (11)</td>
</tr>
<tr>
<td>IPF</td>
<td>81.0%</td>
<td>21 (6)</td>
</tr>
<tr>
<td>CF</td>
<td>83.3%</td>
<td>24 (6)</td>
</tr>
<tr>
<td>CC</td>
<td>87.5%</td>
<td>16 (8)</td>
</tr>
<tr>
<td>COPD</td>
<td>66.7%</td>
<td>12 (11)</td>
</tr>
<tr>
<td>IPF</td>
<td>81.0%</td>
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</tr>
</tbody>
</table>

In the normal healthy volunteer group described by Hayat et al. (2015) there were 87 subjects with 33 having at least one sample Peptest™ positive (37.9%) (1). Median pepsin concentration was 0.0 ng/mL (IQR 0-0) with a mean of 17.0 ng/mL (standard deviation 43.4) suggesting even a large, well-defined normal control group can have pepsin in expectorated saliva but only of low concentration. The patients in this study have significantly greater prevalence of pepsin than the standard control population. This data highlights the requirement for case-controlled studies in lung disease patients.

A subset of patients was noted as to whether they were prescribed proton pump inhibitor (PPI) medication. In the diseases investigated the use of PPI did not impact on the likelihood of detecting pepsin with Peptest™.

Conflict of interest

Vicki Strugala, Radka Bittenglova, Lucie Fremundova, Milos Pešek have no conflicts of interest to report. Peter W Dettmar is managing Director of RD Biomed Ltd.
aspiration of gastric contents using detection of pepsin in expectorated saliva using Peptest™. Pepsin was detected even in patient’s prescribed PPI medication that clearly influenced acid secretion but not reflux of pepsin. Reflux above the upper oesophageal sphincter and into the airways may not be causative of these investigated conditions but the presence of damaging pepsin will certainly be a negative influence that may increase disease severity or reduce the impact of pulmonary medication/therapy.

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References