

## The seroprevalence of *Helicobacter pylori* infection in patients with obstructive sleep apnoea: a preliminary study

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### The seroprevalence of *Helicobacter pylori* infection in patients with obstructive sleep apnoea: a preliminary study

We investigated the seroprevalence of *Helicobacter pylori* in patients with obstructive sleep apnoea. A prospective clinical study consisting of 19 patients, aged 23–72 years with confirmed obstructive sleep apnoea by overnight polysomnography, and 36 control subjects, aged 25–61 years with no history of obstructive sleep apnoea and gastroesophageal reflux complaints, was conducted. Titres of serum *H. pylori* IgG antibody were assayed by a serum enzyme-linked immunoabsorbant assay. The difference between the study and control groups was analysed by chi-squared test. Seventeen of the 19 patients (89.5%) were found to be *H. pylori* positive. However, 21 of the 36 control subjects (58.3%) were *H. pylori* positive. The seropositivity of *H. pylori* in obstructive sleep apnoea patients was found to be significantly higher than the control group ( $P=0.017$ ). The result of our study shows that there is a high association between *H. pylori* infection and obstructive sleep apnoea. This data may be important for future treatment strategies of the disease.

Keywords *Helicobacter pylori* obstructive sleep apnoea gastroesophageal reflux serological tests

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Obstructive sleep apnoea is an important medical condition characterized by cessation of breathing spells during sleep, which is associated with significant cardiovascular morbidity. It has been demonstrated that effective treatment with uvulopalatopharyngoplasty or nasal CPAP reduces the morbidity rates.<sup>1,2</sup>

In recent years, gastroesophageal reflux has been suggested to have a relation with several aero-digestive tract disorders, including obstructive sleep apnoea, asthma, laryngospasm, sudden infant death syndrome, subglottic stenosis, vocal cord nodules, hypertrophy of the base of the tongue, otitis media with effusion, chronic rhinosinusitis, chronic bronchitis, and laryngeal and hypopharyngeal carcinoma without classical symptoms and signs.<sup>3–7</sup>

*Helicobacter pylori* is a microorganism that can cause an acute gastritis which in turn can develop into a chronic form

within 2–3 weeks.<sup>8</sup> *Helicobacter pylori* gastritis is widespread in many countries in the world and also may be one of the most common chronic human infections. The role of *H. pylori* infection in the pathogenesis of gastroesophageal reflux is still controversial. Some studies indicate a protective role, however, others report an improvement of gastroesophageal reflux symptoms after treatment of the infection.

The aim of this study was to investigate the seroprevalance of *H. pylori* infection in adult patients with obstructive sleep apnoea.

### Materials and methods

We prospectively studied 19 patients with obstructive sleep apnoea (three women and 16 men) between the ages of 23 and 72 years (mean age = 48.6 years) and 36 control subjects (10 women, 26 men) with no history of obstructive sleep apnoea (using the Epworth sleepiness scale) and gastroesophageal reflux complaints (including heartburn, dyspepsia, throat clearing, globus sensation and voice quality change were

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questioned) between the ages of 25 and 61 years (mean age = 43.4 years). The diagnostic work-up consisted of a complete medical history, physical examination of the upper airway, blood samples for *H. pylori* IgG antibody and complete overnight polysomnography. Overnight polysomnographic recording (Alice 3; Healthdyne, Pittsburgh, PA, USA) included central and occipital electroencephalogram, submental electromyogram, electrooculogram, electrocardiogram; left and right leg movements (EMG) and respiratory parameters such as oro-nasal flow, thoracic and abdominal movements were recorded, respectively, by thermistor and strain gauges. Arterial oxygen saturation was monitored by pulse oximetry. Apnoea is a cessation of airflow for longer than 10 s and hypopnoea is a 50% reduction in airflow for longer than 10 s. The diagnostic criterion for obstructive sleep apnoea on overnight polysomnography was an apnoea-hypopnoea index of at least 5 episodes/h.

Titres of *H. pylori* IgG antibody were assayed by a serum enzyme-linked immunosorbent assay (ELISA; lot no: L08725; Quorum Diagnostics, Canada). A cut-off value (iu/ml) was determined and IgG levels were accepted as 'positive for *H. pylori*' above the value of 20 iu/ml.

The difference between the study and control groups was analysed by chi-squared test and  $P < 0.05$  was accepted as significant.

## Results

In the obstructive sleep apnoea group, the mean apnoea-hypopnoea index was 29, and all of the patients had three of the gastroesophageal reflux symptoms and signs. We estimated the incidence of seropositivity at 89.5% (17/19) in the obstructive sleep apnoea group and 58.3% (21/36) in the control group. The seropositivity of *H. pylori* in obstructive sleep apnoea patients was found significantly higher than the control group ( $P = 0.017$ ).

## Discussion

*Helicobacter pylori* has been estimated to infect approximately half of the world's population with the majority of them thought to remain asymptomatic. In the United States, 40% of the population may be infected and, in our country, it is reported that the incidence is around 60%.<sup>9,10</sup> The seroprevalence of *H. pylori* in the control group of this study was similar to this data. Human, monkeys and cats are its hosts. Some researchers emphasize that the oral cavity is a reservoir for systemic infections and Unver *et al.*<sup>11-13</sup> found a 57.9% rate of *H. pylori* presence in tonsil and adenoid tissues. Sensitivity and specificity for the *H. pylori* antibody tests (only the serum IgG-based tests have been approved by the FDA) are about 95%.<sup>10</sup> Serological tests are non-invasive, relatively inexpensive and easily performed diagnostic

methods. Serological test results are not affected by prior treatment with antibiotics or proton pump inhibitors but they are less specific than endoscopic or breath tests; a positive titre strongly supports the presence of an ongoing infection, except in the elderly, where titres may be false negative.<sup>14-16</sup> In our study group, we had two patients who were *H. pylori* negative, one of them was a 72-year-old and IgG titres might be false negative.

Gastroesophageal reflux into the laryngopharynx has been implicated as an inflammatory cofactor and possible cause of many adult and paediatric upper airway disorders.<sup>5</sup> There have been studies reporting the presence of significant gastroesophageal reflux in patients with obstructive sleep apnoea. It was also noted that the co-existence of both syndromes in the same patients and nasal continuous positive airway pressure reduced the severity of gastroesophageal reflux episodes.<sup>1</sup> It is widely suggested that obstructive sleep apnoea and gastroesophageal reflux may be an interrelated phenomenon. The same type of patient is predisposed to both conditions with common aetiological factors such as obesity and alcohol use.<sup>1,2</sup> Koufman<sup>17</sup> reported that gastric juice reflux occurring three times a week is sufficient for severe laryngopharyngeal lesions. Two pathophysiological mechanisms have been proposed for the association between gastroesophageal reflux and airway disorders: micro aspiration of gastric contents into the bronchial system and activation of the vasovagal reflex arc.<sup>2</sup>

The role of *H. pylori* infection in the pathogenesis of gastroesophageal reflux is controversial. Epidemiological studies have shown that the prevalence of *H. pylori* infection is no higher in patients with gastroesophageal reflux than in healthy control subjects.<sup>18</sup> Some studies indicate a protective role and reported an increased risk of developing gastroesophageal reflux after eradication of *H. pylori* in patients with duodenal ulcer, however, others report an improvement of reflux symptoms after treatment of the infection.<sup>19,20</sup> Probably, *H. pylori*-positive patients with a duodenal ulcer show a different pattern of gastric acid secretions to those without ulcer disease.<sup>20</sup> In our study, we did not investigate the gastroesophageal reflux incidence in our patient group and also no data as to the prevalence of gastroesophageal reflux in patients with obstructive sleep apnoea has been published. Furthermore, Senior *et al.*<sup>2</sup> found a significant improvement in 30% of patients with obstructive sleep apnoea and gastroesophageal reflux when their complaints were aggressively treated with omeprazole, diet and precautions. Also, Aygenç *et al.*<sup>21</sup> reported a high incidence of *H. pylori* seropositivity in patients with squamous cell carcinoma of the larynx (73.07% in the patient group versus 40.62% in the control group) and concluded that *H. pylori* infection of the upper aero-digestive tract might result in mucosal disruption, allowing for subsequent transformation by known carcinogens such as tobacco and alcohol. Also, Skinner *et al.*<sup>22</sup> demonstrated that *H. pylori* is cytotoxic via a nitric oxide synthase cascade and *H. pylori*

does not appear to colonize the tonsil. They believe that *H. pylori* primes the tonsils by inducing macrophage inducible-nitric oxide synthase expression, and the higher expression in seropositive patients is a reflection of a pro-inflammatory reaction to *H. pylori* that is both local and systemic. It is not obvious whether *H. pylori* in the aero-digestive tract is a result of the disordered epithelium or the causative factor for obstructive sleep apnoea, tonsillitis or laryngeal cancer. This point needs further studies. We believe that gastroesophageal reflux and obstructive sleep apnoea, *H. pylori* and gastroesophageal reflux and *H. pylori*-associated mucosal disruption of the upper aero-digestive tract are interrelated phenomena.

## Conclusion

The 89.5% rate of *H. pylori* seropositivity found in our study shows that there is a high association between *H. pylori* infection and obstructive sleep apnoea. This result may be important for future treatment strategies and understanding of the pathophysiology of the disease.

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