SHORT REPORT

Shift work increases the frequency of duodenal ulcer in *H pylori* infected workers

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Aim: To evaluate whether shift work is associated with an increased rate of peptic ulcer in *H pylori* infected workers.
Methods: During a two year period, consecutive dyspeptic workers underwent non-invasive evaluation of *H pylori* status by means of urea ^{13}C breath test or stool testing. Those testing positive were included in the study and divided into two main categories: day-time workers and shift workers. An upper gastrointestinal endoscopy was performed in all workers, and biopsy specimens were taken from the stomach to confirm the presence of *H pylori* infection (culture and histology).
Results: A total of 247 day-time workers and 101 shift workers were included. The prevalence of duodenal ulcer was significantly higher in shift workers than in day-time workers (29 of 101 *v* 23 of 247; OR = 3.92, 95% CI 2.13 to 7.21), and persisted after multivariate analysis, taking into account possible confounding factors (OR = 3.96, 95% CI 2.10 to 7.47).
Conclusion: Shift work increases the ulcerogenic potential of *H pylori* infection and should be considered a risk factor for duodenal ulcer in infected shift workers. Treatment of infection in this high risk group may improve the health of workers and may reduce the economic impact of peptic ulcer.

Peptic ulcer disease is considered to be strongly linked to shift work including night working.[1] However, most studies regarding this relationship are outdated, based on non-standardised assessment of symptoms, and mainly relying on *x* ray evaluation.[1] More important, no study has evaluated the role of *Helicobacter pylori*, the main causative agent of peptic ulcer disease.[2] On the other hand, the outcome of *H pylori* infection is strongly influenced by host and environmental factors: in fact, although virtually all peptic ulcers are caused by this organism, only a minority of infected subjects develop the disease.

In the present study, we examined whether shift workers infected by *H pylori* are more prone to develop peptic ulcer disease in comparison to infected day-time workers.

METHODS

During a two year period, a pool of primary care physicians involved in an educational programme with our Institution[3] selected all active workers from at least one year who had persistent dyspeptic symptoms (i.e. pain or discomfort centred in the upper abdomen for at least 4 months).

These subjects underwent non-invasive assessment of *H pylori* infection with urea ^{13}C breath test or with stool testing; those testing positive were sent to us for further evaluation. At this time, an occupational physician identified two groups of dyspeptic workers: day-time workers; and workers on either night shifts or rotating shifts that included at least an average of four nights per month during the last year. We considered as day-time workers those regularly working between 6 am and 7 30 pm from at least one year, who had no past history of shift work including night working. Night-time work was defined as a shift including at least 3 hours between midnight and 5 am. Both groups were considered for upper gastrointestinal endoscopy. Exclusion criteria for endoscopy were: previous endoscopic evaluation, regular non-steroidal anti-inflammatory drug intake, consumption of proton pump inhibitors or H_2 receptor antagonists during the month before endoscopy, previous *x* ray diagnosis of peptic ulcer, and antibiotic intake after non-invasive diagnosis of *H pylori* infection. A standard upper gastrointestinal endoscopy was performed. The endoscopist was unaware of whether the patient was a shift worker or a day-time worker. During endoscopy, three biopsy specimens were taken from the gastric antrum, and three from the gastric body. At each site, two biopsy specimens were utilised for histological assessment of inflammation and of *H pylori* infection, and one was utilised for culture and urease testing. Patients were considered infected if culture and/or urease testing plus histology tested positive. Details on the performance of histology and culture have been given elsewhere.[4]

Data are expressed as mean $\pm$ standard deviation. Univariate analysis and multiple logistic regression, including factors possibly affecting the risk of peptic ulcer were used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for peptic ulcer associated with shift work. All analyses were performed with SPSS release 13 software.

RESULTS

Overall, 941 workers were considered; 395 of them tested negative at the non-invasive testing for *H pylori* infection, and were therefore excluded from the study. Among the remaining 546 workers, 303 were classified as day-time workers, and 132 as shift workers with a job schedule including at least four nights per month. The remaining 111 workers with a different job schedule were excluded. Eighty one patients did not perform endoscopy because they did not meet the inclusion criteria (39 patients among day-time workers and 28 among shift workers) or because they refused the procedure (13 patients among day-time workers and two among shift workers). Thus, endoscopy was performed in 251 day-time workers and 102 shift workers. After endoscopy, four additional day-time workers and one shift worker were excluded, since they were *H pylori* negative at invasive testing. Thus, our final analysis included 247 day-time workers and 101 shift workers.

The two groups were similar with respect to age (39.13 ± 9.88 *v* 40.54 ± 10.20 years), prevalence of male sex (66.3% *v* 57.9%), and familial history of peptic ulcer disease (19.8% *v* 17%), whereas active smokers were more frequently detected among shift workers than among day-time workers (38% *v* 25.9%; OR 1.72, 95% CI 1.05 to 2.82; p = 0.04).

Table 1 Odds ratio for the development of duodenal ulcer in day-time workers and shift workers after adjustment for possible confounding factors

Variable	OR*	95% CI
Age	0.98	0.96–1.01
Sex	1.38	0.82–2.30
Smoking	1.63	0.97–2.76
Familial history	1.02	0.55–3.41
Prevalence of duodenal ulcer	3.96	2.10–7.47

*ORs are adjusted with each other.

The prevalence of duodenal ulcer was higher in shift workers than in day-time workers (29/101, 28.7% *v* 23/247, 9.3%; OR 3.92, 95% CI 2.13 to 7.21; $p < 0.0001$) and persisted after multivariate analysis, taking into account possible confounders: OR 3.96, 95% CI 2.10 to 7.47 (table 1).

No significant difference in the prevalence of duodenal ulcer was observed between smokers and non-smokers (day-time workers: 7.8% *v* 9.8%, OR 0.77, 95% CI 0.28 to 2.11, $p = 0.63$; shift workers: 34.2% *v* 25.3%, OR 1.52, 95% CI 0.69 to 3.64, $p = 0.34$).

Gastric ulcer was diagnosed in 4/101 shift workers (3.9%) *v* 3/247 day-time workers (1.2%) ($p = 0.11$).

In both groups, we did not detect any significant association in the prevalence of peptic ulcer with a particular job; furthermore, the difference between shift workers and day-time workers was present within the same job (table 2).

Finally, the prevalence of peptic ulcer among shift workers was higher in those working for at least seven nights per month during the last year (10/21, 47.6%) in comparison to other shift workers (18/80, 22.5%) (OR 3.13, 95% CI 1.14 to 8.54; $p = 0.04$)

Table 2 Prevalence of duodenal ulcer according to different types of work in day-time workers and in shift workers

Job	Peptic ulcer/shift workers	Peptic ulcer/day-time workers
Industry workers	8/28 (28.6%)	2/16 (12.5%)
Drivers	3/10 (30%)	0
Healthcare workers	7/18 (38.8%)	3/35 (8.6%)
Police officers	3/13 (23.1%)	1/11 (9.1%)
Telecommunication or media workers	2/16 (12.5%)	1/26 (3.8%)
Retailers	2/5 (40%)	4/31 (12.9%)
Teachers	0	2/24 (8.3%)
Employees	0	8/86 (9.3%)
Others	4/11 (36.3%)	1/28 (3.5%)

DISCUSSION

We examined a population of *H pylori* infected dyspeptic workers, and found that the prevalence of duodenal ulcer was strongly increased in shift workers in comparison to day-time workers; furthermore, a positive relationship between the number of nights worked per month and the risk of peptic ulcer was detected. This finding may have relevant implications in occupational medicine, since it identifies *H pylori* positive dyspeptic shift workers as a high risk group for peptic ulcer disease. Because this disorder is an important cause of absence from work,[5] strategies aimed at its prevention in high risk groups may have relevant clinical and economic implications. Further support to this consideration is given by the fact that the prevalence of *H pylori* infection is probably increased in shift workers.[6]

We feel that treatment of infection is a better strategy for preventing peptic ulcer disease in shift workers. In fact, *H pylori* eradication is relatively easy, requiring a one week course of antibiotic therapy, and recurrences are rare after successful treatment. This approach does not necessarily require changes in work schedule, since in spite of the persistence of any co-factor, the development of peptic ulcer is practically impossible in the absence of *H pylori* infection.

Thus, we recommend screening procedures for *H pylori* infection for dyspeptic shift workers. According to current guidelines, infection in subjects less than 45 years old, without alarming symptoms, can be confidently eradicated without further invasive diagnostic procedures.[7] In this context, occupational physicians may play a major role for the application of this preventive strategy in shift workers. The usefulness of this approach in day-time workers is much less certain, because dyspeptic symptoms disappear after eradication only if they are induced by a duodenal ulcer;[8] given the relatively low rate of duodenal ulcer in this group, the impact of screening and eradication is probably negligible in an economic perspective.

Previous studies on the relationship between peptic ulcer and shift work did not control for *H pylori* infection:[1] this fact reduces the reliability of these data, since the disease is strongly linked to infection; thus, differences in the prevalence of infection between cases and controls may result in spurious associations. Furthermore, effective preventive measures cannot be taken without knowing *H pylori* status.

According to the accepted model of *H pylori* related ulcer, the organism first colonises the gastric antrum, inducing the so-called antrum predominant gastritis. This kind of gastritis increases acid output, which induces a gastric metaplasia in the duodenum; the presence of gastric mucosa in the duodenum allows colonisation of the organism, and the subsequent development of duodenal ulcer.[9] Shift work may interact with this pathophysiological model. Indeed, long term stress and nocturnal sleep deprivation, typically associated with shift work,[10] may increases gastric acid secretion,[11] and reduce mucosal defence.[12]

The study has some limitations. In fact, we cannot exclude the possibility that uncontrolled factors increasing the rate of duodenal ulcer, such as genetic predisposition or associated diseases, may have affected our findings. Furthermore, shift workers are largely a self selected population and therefore inherent differences unrelated to shift work itself may be present.

In conclusion, this study supports the findings of previous studies that have reported a higher rate of duodenal ulcer in shift compared to day workers, and confirms that these results are not only due to the differential rates of *H pylori* infection in these two groups of workers. *H pylori* eradication, by reducing the risk of peptic ulcer in shift workers, may also have relevant economic consequences.

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