Factors Responsible for the Increasing Incidence of Oesophageal Adenocarcinoma

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**Abstract**

Amongst white population of developed countries, the prevalence of oesophageal adenocarcinoma has dramatically increased during the last four decades. During this period, the increased damage to the oesophageal mucosa with gastroesophageal reflux could result from increased acid output (due to absence of Helicobacter pylori in the gastric mucosa with excellent sanitation) and/or increased frequency of reflux due to an “epidemic” of overweight (65% of the population). The most important environmental factors, responsible for the fastest increasing cancer in humans, are discussed. ©

**INTRODUCTION**

In developed countries (North America, Europe, Australia), the prevalence of oesophageal adenocarcinoma (OAC) has dramatically increased during the last four decades. Of total oesophageal carcinoma, OAC constituted only 15% in 1970 – 80 and about 60% in 2000. In white population, OAC had increased four times during this period. The annual incidence of OAC is 3.6/100,000 in white men and 0.8/100,000 in African – American. The OAC is the fastest increasing cancer in humans. It could be due to environmental factors only, as hereditary factors do not alter in such a short period. The most important environmental factors, which probably are responsible for this “epidemic” of OAC in Western countries, are discussed.

Increasing incidence of OAC, could be secondary to the increasing prevalence of Barrett’s oesophagus (BO) as a result of enhanced damage with gastroesophageal reflux (GER). The increased damage with GER during the last four decades, could result either from the increased acid in the stomach (absence of Helicobacter pylori (HP)) and/or the increased frequency of GER due to obesity.

**Absence of Helicobacter pylori in the gastric mucosa and Gastroesophageal reflux**

About half the world’s population is infected with HP and faeco-oral route is the major mode of its transmission. In adult population, HP prevalence is about 90% in developing countries (India, China, Africa) and less than 50% at 50 years of age in developed countries (North America, Europe, Australia). These differences are explained on the basis of, poor and good sanitation-hygiene, in developing and developed countries respectively.

With excellent sanitation, HP exposure in the western population is minimal. During the last four decades, the prevalence of HP in the gastric mucosa has further steadily decreased in developed countries. The decreasing prevalence of HP in the developed countries is reflected with the decreasing prevalence of gastric carcinoma and duodenal ulcer and the increasing prevalence of endoscopic oesophagitis (EO), BO and OAC. In Japan, North America, India, the prevalence of gastric carcinoma was 100, 13, 9 per 100,000 population in 1970 and 50, 7.5, 4 in 2000 respectively, indicating a decreased prevalence of HP due to improved sanitation-hygiene. In an Asian city Singapore (1992-2001), the prevalence of HP on rapid urease test decreased from 40 to 28% and the prevalence of EO increased from 3.9 to 9.8% in patients undergoing endoscopy.

Since HP causes chronic gastritis in the body mucosa and diminishes acid secretion, absence of HP results in higher acid secretion in the population. The higher concentration and volume of reflux in the oesophagus, increases the damage in the oesophageal mucosa, resulting in the higher incidence of EO, BO, OAC. Both the short (< 3 cm) and the long (> 3 cm) segment BO increases the risk of OAC. BO increases the risk of OAC 30 times than in general population. The prevalence of EO, BO is significantly lower in black than in white population.

The protective role of HP in reducing the incidence of EO, BO, OAC in developing countries has been emphasized. In Asia, BO (and OAC) is
uncommon as the values of maximal acid output are low. In duodenal ulcer patients, the values of maximal acid output were reported to be significantly lower (approximately 25.0 meq/hr) than those reported in patients from developed countries (37.5 meq/hr); the values of maximal acid output were more than 40 meq/hr in 5% of patients from Mumbai and in 40% of patients from developed countries. In the gastric mucosa of Indian patients, the high prevalence of HP and for longer duration of time (due to early exposure in childhood), explains these differences.

**Obesity And Gastroesophageal Reflux**

Amongst adult population in North America, 65% are overweight, 30% are obese (body mass index: BMI >30 kg/m²) and 5% are morbidly obese (BMI > 40 kg/m²). GER symptoms are more frequent in obese than in lean subjects and showed a good correction with BMI both in normal weight and overweight subjects; for every 5kg/m² higher BMI, hospitalization for GER symptoms increased by 22%. Reflux symptoms decrease after gastric bypass surgery.

Amongst 93 control subjects and 36 patients with BO, visceral adipose tissue and subcutaneous adipose tissue were measured on computed tomography between L₁-L₅ level. Visceral adipose tissue scores were significantly higher in BO patients than in controls but subcutaneous adipose tissue values were comparable in these two groups. GER symptoms occurs more frequently with raised intra-abdominal pressure due to visceral adipose tissue. BMI values were also significantly higher in BO patients than in controls. Patients with EO showed a significantly higher intake of fat and lower intake of fiber.

Absence of HP in the gastric mucosa and obesity, both contribute to increased damage with GER, causing a higher incidence of EO, BO and OAC. The lack of exposure to HP, with improved sanitation, affects the vast majority of the population while obesity affects about 30% of the adult population in western countries. Absence of HP in the gastric mucosa is hence far more important factor than obesity, in increasing the incidence of OAC in developed countries.

**Conclusions**

“The only good HP is a dead HP” and “test and treat” (eradicate HP whenever detected), are dangerous concepts. The eradication of HP should be restricted to patients with peptic ulcer and mucosa associated lymphoid tissue gastric lymphoma. Human race should appreciate the beneficial role of different bacteria throughout the gastrointestinal tract. Deleterious effects of obesity on different organs are too well known and to this list, oesophagus needs to be included.

**References**

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