Aging and the alimentary tract

The aging stomach: implications for NSAID gastropathy

Over 30 million people worldwide use non-steroidal anti-inflammatory drugs (NSAIDs) daily, and nearly 50% of these NSAID users are elderly. Numerous human studies have shown that the use of NSAIDs is associated with various gastroduodenal mucosal lesions, sometimes collectively referred to as NSAID gastropathy, and that NSAID gastropathy and its life-threatening complications occur primarily in elderly patients. Overall, the use of NSAIDs increases the risk of peptic ulcer disease, ulcer complications (haemorrhage and/or perforation), and death from ulcer by a factor of between 2 and 4. In the United States alone, medical costs attributable to NSAID gastropathy and its complications exceed $4 (£2.4) billion a year. Although increased NSAID use among the elderly is an obvious risk factor, epidemiological data suggest that aging is an independent risk factor for the development of NSAID gastropathy and its complications. The aim of this article is to review recent developments in the area of age related changes in gastric physiology that may predispose the elderly to NSAID gastropathy. A better understanding of the age related changes in gastric mucosal functions will help us to develop novel interventions for the treatment and prevention of NSAID induced gastrointestinal injury in susceptible elderly people.

Mechanisms of NSAID induced gastric mucosal injury

The mechanisms by which aspirin and other NSAIDs produce acute and chronic gastroduodenal mucosal injury are incompletely understood. In general, gastric mucosal injury is thought to result when aggressive luminal factors (such as acid and pepsin) overwhelm local mucosal protective factors (such as mucus and bicarbonate). Results from animal studies suggest that the production of mucosal lesions by aspirin is a result of two independent mechanisms: (a) cyclooxygenase inhibition by aspirin; and (b) topical effects induced by salicylate, the product of aspirin deacetylation. The salicylate induced toxic effects include changes in transmembra...
epithelial cells compared with young male rats, and that this change is associated with gastric mucosal erosions in aged rats. Furthermore, the rate of proliferation of stem cells in the neck of the gastric glands is reduced in aged rats. Majumdar et al have reported that aged rats are more susceptible to hypertonic saline induced acute gastric injury, and that the magnitude of gastric mucosal proliferative response is higher in young rats than in aged rats. Subsequent mechanistic studies have demonstrated that aging is associated with diminished regenerative capacity of gastric mucosa that has been damaged by hypertonic saline; and this age related deficiency in mucosal repair is secondary to reduced expression of various growth factors (such as transforming growth factor β) and growth factor receptor related enzymes (such as tyrosine kinases) in the stomachs of aged rats.

Gastric mucosal blood flow plays an important role in maintaining the gastric mucosal integrity and contributing to mucosal repair by supplying oxygen and nutrients and by removing injurious agents and phlogogenic substances. Although there is little published information on the effects of aging on gastric mucosal blood flow in humans, two recent animal studies have shown that aging significantly affects gastric blood flow. Lee has reported that aging is associated with a significant decline in basal gastric blood flow, whereas there is no significant difference in acid induced increases in gastric blood flow between young and aged rats. In another study, Miyake et al reported that gastric mucosa of aged rats is more vulnerable to acid back-diffusion following acute mucosal injury because of dysfunction of gastric mucosal blood flow responses mediated by capsaicin sensitive sensory neurons in the presence of mucosal disruption and acid back-diffusion. Taken together, recent animal studies suggest that aging is associated with selective and specific changes in gastric mucosal defensive mechanisms that may predispose aged animals to gastric mucosal injury.

Conclusion
A review of human and animal studies indicates that while there is little or no change in gastric luminal aggressive factors with normal aging, advancing age is associated with significant alterations in various gastric mucosal defence mechanisms and diminished responsiveness to injury. These age related changes in gastric mucosal defence may explain the predisposition of elderly people to gastric ulcer disease, especially in the setting of NSAID use.
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