OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference on
Gastroenterology & Urology
June 10-12, 2013 Hilton Chicago/Northbrook, USA

Chemoprevention in Barrets Esophagus

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Barret's Esophagus (BE) foreruns Esophageal Adenocarcinoma (EAC) by 0.5% annual risk, the malignancy conversion diagnosis bringing high levels of morbidity and mortality, and statistically being the fourth most common gastrointestinal malignancy in the United States. Squamous to Columnar metaplasia presence compared to general population, increases metastatic risk 30- to 125-fold specifically for EAC. Normally present esophageal squamous epithelium being exposed to pancreatic, intestinal and gastric secretions abnormally via GERD mechanisms causes intestinal differentiation via inhibition of Epidermal Growth Factor Receptor, and a Protein Kinase linked Enzyme, Akt. Through upregulation of p50 subunit of NFKB1, then activation of CDX2 gene, responsible for intestinal enzyme Guanylate Cyclase 2C. This also explains involvement of HER2/neu, and the specificity of Anti-HER2 drug Trastuzumab. Current surveillance techniques for BE patients is through serial endoscopy monitoring with tissue sample histopathological assessments. Such level of invasiveness and discomfort to patients produces poor compliance, thus necessitating progressive efforts towards chemoprevention, effectively reducing cost to patient and healthcare infrastructure through reduced serial endoscopy, and diminished cancerous EAC progression through pharmacoreduction of its precancerous state. Drugs targeting H+/K+ ATPase pump on gastric Parietal Cells:Proton Pump Inhibitors (PPIs) are commonly prescribed for patients with BE to provide suppression of gastric acid. Acid suppression is being studied in relation to BE. Few retrospective cohorts showed that PPI use has been associated with a reduced likelihood of progression of BE to cancer, however this has not yet been adequately corroborated by sufficient statistics. There is limited observational data demonstrating association of PPI use and the reduced incidence of dysplasia in BE. NSAIDS are also of note in BE. Chronic inflammation resulting from chronic acid reflux increases cyclooxygenases and associated cellular proliferation, apoptosis and angiogenesis. COX inhibitors also may play a chemopreventive role in BE. Studies have shown that the COX 2 increase in BE may be counteracted, at least somewhat by specific inhibitors. However COX 2 inhibitors have significant side effect profiles which may outweigh the benefits. Statins have also been disappointing in BE. Other agents actively investigated currently are troglitazone and all-transretinoic acid. Large prospective studies are yet to be carried out before definitive chemopreventive strategies are devised.

Biography

Sandeep Pericherla is a graduate of Sri Ramachandra Medical School, Chennai. He is currently applying for residency programs in the USA. He has a sincere passion for teaching and sharing his medical experiences with anyone who may benefit.

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