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The Impact of HAART in the Gastrointestinal Tract

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Abstract

Discovery of HAART announced the transformation of HIV infection from a deadly illness to a chronic manageable disease. The objective of this study is to show the impact of HAART in the GI tract. This study was conducted through online research using the database of NCBI. Multiple studies have shown that HAART has changed the clinical presentation of gastrointestinal disorders; oral lesions have decreased more than 30%; opportunistic disorders decreased from 69% to 13%. HIV patients with diarrhea receiving PI had a higher rate of response; 62% versus 33.5%. This population is at increased risk for developing malignancies of the GI tract; both proximal and distal. Even though with the introduction of HAART, patients with HIV have improved life expectancy rates and survival, public health strategies to improve cancer screening are needed.

Keywords: HIV; HAART; Gastrointestinal system; Opportunistic disorders; Colorectal cancer

Abbreviations:

AIDS: Acquired Immunodeficiency Syndrome; CMV: Cytomegalovirus; CRC: Colorectal Carcinoma; HAART: Highly Active Antiretroviral Therapy; HIV: Human Immunodeficiency Virus; HPV: Human Papilloma Virus; NHL: Non Hodgkin Lymphoma; NCBI: National Center for Biotechnology Information; OD: Opportunistic Disorders; PI: Protease inhibitors; SCCA: Squamous Cell Carcinoma

Introduction

The discovery of HAART announced the transformation of HIV infection from a deadly illness to a chronic manageable disease. HAART which is defined as a combination of protease inhibitor and non-nucleoside analog reverse-transcriptase inhibitor can increase the absolute number of CD4 count, suppress viral load, increase survival and improve the quality of life.

The objective of this study is to show the impact of HAART in the GI tract. This study was conducted through online research using the database of NCBI.

The gastrointestinal lymphoid associated tissue is one of the biggest reservoirs of HIV and the GI tract is a common site for clinical expression. Complications in the GI tract attributable to HIV vary from infections to malignant diseases with the opportunistic disorders being the most common.

Oral Lesions

Oral Candidiasis is most commonly associated with *Candida Albicans*. It can clinically present in two forms: pseudo membranous and erythematous Candidiasis. The pseudo membranous type represents as creamy white, removable plaques on the oral mucosa that are caused by overgrowth of fungal hyphae mixed with desquamated epithelium and inflammatory cells. This type of candidiasis is the most closely related to poor immunologic status. Erythematous candidiasis appears as flat, red patches of varying size that commonly occurs on the palate and the dorsum of the tongue [1,2].

A study that included 72 patients receiving HAART and CD4 count less than 499 was conducted to study the prevalence of oral lesions. A marked decrease was observed in oral candidiasis, especially in the pseudomembranous type. The improvement in these patients showed that the poor immunologic status was not reached. The study not only showed a marked decrease in oral candidiasis in patients under HAART therapy but also, in Hairy leukoplakia which is strongly related to immunologic status. A major drop was also noticed in the incidence of both non-Hodgkin lymphoma and Kaposi's sarcoma of the mouth [1].

Another study [2] examined 154 AIDS patients receiving HAART. This study showed that the prevalence of oral lesions, particularly pseudomembranous candidiasis, herpes simplex labialis, Kaposi sarcoma and periodontal disease has decreased more than 30% after the discovery of HAART.

Esophageal and Stomach Lesions

HIV patients usually complained of dysphagia, odynophagia or both. The most frequent cause of these complains is Candidal Esophagitis [3]. The Belgium study in 2010 showed that the prevalence of Candida esophagitis decreased in the HAART era. A significant association was found between the frequency of Candida, CD4 count and the viral load. A reduced incidence in Kaposi Sarcoma was also observed in the HAART era. This type of malignancy occurs in low CD4 count. A higher rate was observed for both symptoms and endoscopic findings of GERD. This study found an association between the increases in frequency of both GERD and HP infection and the increase in CD4 count [4]. The most common viral esophageal disease is CMV and is identified in 10-40% of biopsies of esophageal lesions [3].

CMV Esophagitis presents with ulcers that are usually found in the middle and distal esophagus. Gastric CMV infection most commonly is presented with erosions, ulceration and hemorrhage.

Werneck-Silva [11] studied the role of EGD in diagnosing OI in HIV patients. A normal appearing mucosa has a good correlation with the absence of opportunistic infections. In this prospective study where 1010 patients were examined a pathogen was found in only one patient. Patient undergoing HAART therapy most often complain of dyspepsia, nausea, vomiting. This mostly occurs because HAART itself causes an increase in gastric acidity. A study [5] with 690 patients was conducted to evaluate the correlation between dyspepsia and OI of the GI tract. The patients were divided in two groups: 500 of the patients were classified as no dyspeptic and 190 of them were classified as dyspeptic. Dyspepsia as a result of OI was found in only 1.6% of the patients, but no correlation was proved. Another study [6] examined with upper endoscopy 528 patients complaining of dyspepsia. The patients were classified in two groups according to their immunologic status; patients with CD4 count less than 200 and patients with CD4 count more than 200. The study showed that the endoscopic findings were not related to AIDS. Also, there was no difference between the two groups in the endoscopic findings according to the CD4 count.

Diarrhea

Diarrhea in HIV patients can be due to different causes: viral, bacterial, opportunistic pathogens or as a result of HAART therapy. Before the discovery of HAART diarrhea was reported in 50% of the patients [7]. Common bacterial pathogens are: *Campylobacter, Clostridium difficile, E.coli, Salmonella, Shigella*. The most common opportunistic pathogen of diarrhea in patient with HIV is CMV. This pathogen can affect the GI system from mouth to anus. CMV can represent itself as a colitis associated with fever, crampy abdominal pain and often bloody stool. CMV diagnoses require multiple biopsies of the colon. Other opportunistic pathogens of diarrhea in GI are; *Cryptosporidium, Microsporidia, Mycobacterium avium* and *intracellulare*. Bini [15] studied the effect of Protease inhibitor in patient with diarrhea. This study utilized the medical records from October 1993-1996 of Bellevue Hospital. Only the patients presented after December 1995 received Protease inhibitors. The study showed that the patients receiving PI had a higher rate of response: 62% versus 33.5%. Protease inhibitors were associated with a significant decrease in stool frequency, increase in weight, decrease in recurrence and a longer mean of survival.

Opportunistic Disorders

A study published in the American Journal of Gastroenterology studied the prevalence of OD in HIV patients before and after the discovery of HAART.

A hundred and sixty six patients were identified and 279 upper EGD and colonoscopy were conducted. OD occurred in 91% of patients with no therapy; in 35% of patients with monotherapy; in 57% of patients with combination therapy without PI and in 30% of patients receiving HAART. The OD decreased from 69% to 13% ($p<0.01$) [14].

Malignancy

Patients with AIDS are at increased risk of developing GI malignancies; both proximal and distal. An increased risk is noticed for esophageal and stomach malignancies and NHLs. The HIV/AIDS Cancer Match study [13] in which 596,955 patients were involved, utilized the data collected from 1980 to 2007 for 16 US population-based HIV and AIDS and cancer registries. This study compared the risks of stomach and esophageal malignancies between people with AIDS and the general population. The study showed that the people with AIDS were at increased risk for carcinomas of the esophagus (SIR, 1.69; 95% confidence interval [CI], 1.37-2.07; n=95) and stomach (SIR, 1.44; 95% CI, 1.17-1.76; n=96). Risk was increased for esophageal adenocarcinoma (SIR, 1.91; 95% CI, 1.31-2.70) and squamous cell carcinoma (SIR, 1.47; 95% CI, 1.10-1.92). After the discovery of HAART the risk of NHLs had decreased from 1980 to 2007, but the risk of developing esophageal and stomach malignancies remains high. Approximately 40% of HIV patients develop cancer; most common being Kaposi Sarcoma and the second most common being NHL. CRC is the third leading cause of death due to cancer in both genders. The pathogenesis of Colon CA in patients with HIV is unclear. Colon CA presented in earlier ages in HIV patients is more advanced than in older ages [9]. Only one study to date has investigated the colorectal screening rates in patients with HIV [8]. The study included patients 50 years or older who were referred for flexible sigmoidoscopy between January 2001 and June 2002. Men comprised 97% of the population. According to the study, patients with HIV were less likely to undergo any colorectal screening examinations compared to patients without HIV. Even though the introduction of HAART, have improved life expectancy rates and survival, more studies need to be done to obtain better data in order to observe a reliable increased or decreased risk of CRC. Also, cancer screening strategies need to be improved in this population.

A very common problem in HIV patients is HPV related carcinoma. The incidence of SCCA has not been impacted by HAART. Hammad [12] shows that its incidence is expected to increase during the HAART era. SCCA occur at a younger age; 47 versus 57; occurring in 89% of the cases in HIV positive patients versus 37% in HIV negative patients.

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