Background

The advent of highly active antiretroviral therapy (HAART) has significantly reduced HIV-related morbidity and mortality among people living with HIV/AIDS. However, conflicting data exists about effectiveness of HAART in reducing disease progression among individuals coinfected with Hepatitis C virus (HCV). Our objective is to assess rates of AIDS-defining illnesses (ADIs), among HIV coinfected and HIV mono-infected individuals in a Canadian cohort of naïve patients initiating HAART.

Methods

This study was conducted within the Canadian Observational Cohort (CANOC) Collaboration, which is comprised of eight cohorts across Ontario (ON), British Columbia (BC) and Quebec (QC). Eligibility criteria for inclusion in CANOC are: documented HIV infection; residence in Canada; aged 19 years and over; initiation of three or more antiretroviral drugs for the first time (i.e. ART-naive HAART start) on or after January 1, 2000; and a documented HIV-1 RNA measurement and CD4 cell count within 6 months before the start of therapy.

HCV co-infection was identified by self-reports, HCV antibody+ and/or PCR+ tests. In univariate analysis, Chi-square tests were used for categorical variables, and Wilcoxon rank sum tests for continuous variables. ADIs were diagnosed according to Centers for Disease Control and Prevention criteria and were classified into a priori groups according to etiology. Generalized Estimating Equation (GEE) Poisson regression models were used to compare rates of ADIs between HIV co-infected and HIV mono-infected individuals after adjusting for other covariates including geographic region, age, gender, CD4 count at HAART initiation and being on HAART.

Results

In total, 4,790 CANOC participants initiated HAART between January 2000 and February 2009. A total of 2,706 participants, with HIV data, were included in the analysis:

- 768 (28%) were HIV co-infected and 1,938 were HIV mono-infected individuals. The event rate for all ADIs was 3.08 (95% confidence interval [CI] = 2.72, 3.48) per 100 person-years.
- Of the total participants, 1,020 (38%) had at least one treatment interruption. Treatment interruptions varied by HCV status, with 441 (57%) of HIV co-infected and 579 (30%) of mono-infected participants reporting interruptions (p < 0.0001). Median length of treatment interruptions was 77 days (interquartile range [IQR] = 44 - 208) for HIV co-infected and 63 days (IQR = 36 - 157) for mono-infected individuals.
- A total of 243 ADI events were reported within the sample of 2,706 participants.

Table 1 summarizes the baseline demographic and clinical characteristics of the CANOC participants by HCV co-infection status. HCV co-infected participants were more likely to be female, Aboriginal, from BC, current or past IDU, to have had a longer period of time since HIV diagnosis, and to have had a CD4 cell count < 200 cells/mm³.

Table 2 describes the crude rates of ADIs of each type; by HCV status and baseline CD4 level. Overall, 243 ADIs were recorded, 81 among the 768 HIV co-infected participants and 162 among the 1,938 HIV mono-infected participants. The event rate for all ADIs was greater in those with HCV co-infection, irrespective of CD4 count cell class status.

Table 3 displays the univariate GEE Poison Regression models for rate of ADIs per person-year. HCV status was associated with increased risk of all ADIs (Rate ratio = 1.38, 95% confidence interval [CI] = (1.01, 1.88), p = 0.03). Older age at HIV diagnosis, history of ADI prior to HAART initiation, IDU, heterosexual status and higher baseline VL, while baseline CD4 < 200 cells/mm³ and being on HAART were associated with decreased risk of ADIs.

Table 4 describes the multivariable GEE Poison models for rate of ADIs per person-year. After adjusting for age, region, baseline CD4 count, baseline viral load and being on HAART, HCV co-infection was not associated with any combination of ADIs (RR = 1.11, 95% CI = (0.79-1.56), p = 0.56). However, HCV remained associated with an increased risk of mycotic infections after adjusting for the other covariates (RR = 1.96, 95% CI = (1.07-3.59), p = 0.03).

Discussion

HCV co-infection was associated with an increased incidence of ADIs and specifically bacterial, mycotic infections and HCV-related mortality. However, after adjusting for treatment interruptions, HCV only remained significantly associated with an increased rate of mycotic infections. Our analysis suggests that variables associated with HCV, including poorer retention on HAART rates, and not HCV itself, are primarily responsible for increased rates of ADIs among coinfected individuals. Our analyses carry important implications with regards to clinical management of patients co-infected with HIV and HCV:

- Clinicians caring for HIV co-infected individuals should ensure patient access to structural and psychological supports that promote adherence to HAART.
- Given the evidence of immunological vulnerability of HCV co-infected individuals this project was funded by an Emerging Team Grant from the Canadian Institutes of Health Research, and is supported by the CTN. For more information about CANOC, please visit www.canoc.ca