

Assessment of Monocyte Activation and Systemic Inflammation Markers in HIV-positive Opioid Users

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BACKGROUND

With increased life expectancy for treated HIV-positive patients, non-AIDS events and substance use have become especially relevant sources of morbidity and mortality. Chronic inflammation is thought to be a driver of non-AIDS events. We hypothesize that opioid use increases intestinal permeability and bacterial translocation from the gut into blood and leads to increased systemic inflammation that may increase morbidity and mortality. We also hypothesize that this effect is moderated by liver disease (liver fibrosis, hepatitis C, hepatitis B).

Objective

Investigate associations between opiate use and levels of monocyte activation and systemic inflammation markers in HIV-positive patients, including the moderating effect of liver diseases.

STUDY DESIGN & METHODS

An exploratory analysis of data from the Russia ARCH observational cohort. 351 HIV-positive antiretroviral therapy-naive individuals followed over two years. Plasma levels of sCD14 (**primary outcome**), IL-6 and D-dimer (**secondary outcomes**), HIV viral load, and CD4 count were evaluated at baseline, 12 and 24 months.

sCD14, IL-6, D-dimer



Main independent variable: data on opioid use (self-report). Participants were categorized into 3 groups according to their history of opioid use:

Current opioid use	Prior opioid use	Never opioid use
• n=121	• n=186	• n=44
• last opioid use within past 30 days	• no use in past 30 days	• never opioid use

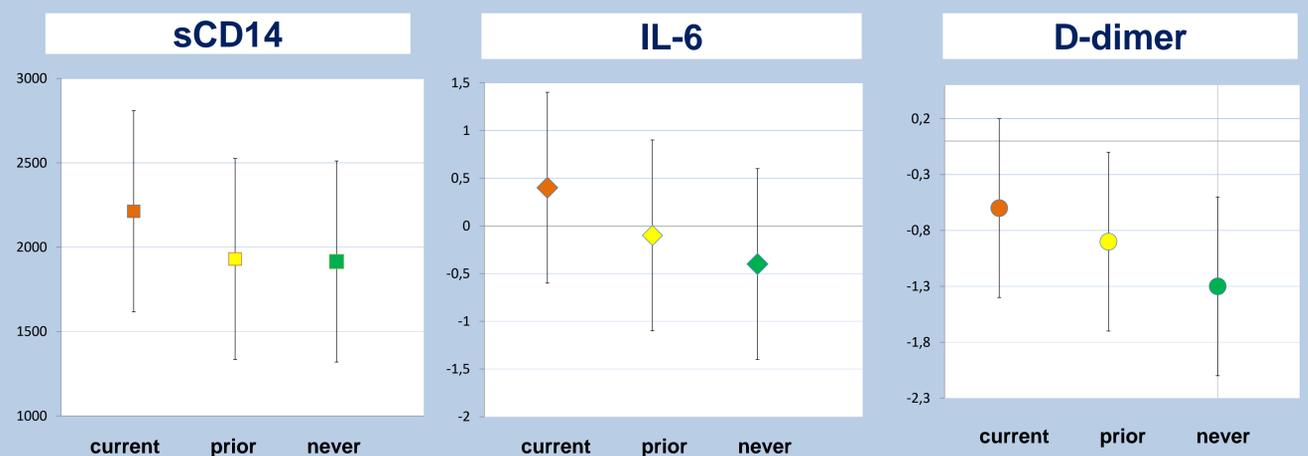
Statistical analysis. Linear mixed effects models were used to evaluate the associations between opioid use and the biomarkers.

Potential effect modifiers: liver fibrosis, hepatitis C, hepatitis B. Liver fibrosis was evaluated by FIB-4 score and dichotomized at 3.25: no advanced fibrosis/cirrhosis at <3.25 and advanced fibrosis/cirrhosis at ≥3.25

RESULTS

Participants' mean age was 34 years old with no significant differences between groups, 71% were male, BMI mean was 22.9. In overall sample HIV-infection had been diagnosed with a mean of 7 years. There were no significant differences in peripheral CD4 T-cell count (mean - 533[297] cells per uL) and HVL in plasma (mean 19953 [12.6] copies/ml) between groups.

At baseline participant with current opioid use had higher sCD14 (2213 [596] ng/mL, $p=0.0001$) levels than participants who reported 'prior' (1930 [597] ng/mL), or 'never' (1915 [577] ng/mL) opioid use (Picture 1). Also higher log-transformed IL-6 (0,4 [1,0] pg/mL; $p<0,0001$) and D-dimer (-0,6 [0,9] ug/mL; $p<0,0001$) levels were shown in participants with current use, compared to those with 'prior' (-0,1 [1,0] pg/mL and -0,9 [0,8]) and 'never' (-0,4 [0,7] pg/mL and -1,3 [0,7] ug/mL) use (Picture 2,3).



Picture 1. Baseline sCD14, M(SD), ng/m

Picture 2. Baseline Log IL-6, M(SD), pg/mL

Picture 3. Baseline Log D-dimer, M(SD), ug/mL

In adjusted models, compared to participants who never used opioids, sCD14 levels were significantly higher among those with current use (adjusted mean difference 259.5 ng/ml [95%CI: 77.0, 441.9], $p=0.008$) but not prior use (adjusted mean difference 116.7 [-54.4, 287.7], $p=0.170$). IL-6 and D-dimer were higher among those with current and prior opioid use (Table).

We did not detect any interaction effects from liver diseases.

Table. Association between opioid use category and plasma concentrations of sCD14, IL6 and D-dimer. Linear mixed effects model

	sCD14 Adjusted Mean Difference (95% CI)	IL-6 Adjusted Ratio of Means (95% CI)	D-dimer Adjusted Ratio of Means (95% CI)
current opioid use (within past 30 days)	259.5* (77.0, 441.9) $p=0.008$	2.130* (1.576, 2.879) $p<0.001$	2.062* (1.519, 2.799) $p<0.001$
prior opioid use	116.7 (-54.4, 287.7) $p=0.170$	1.333* (1.005, 1.767) $p=0.046$	1.682* (1.257, 2.250) $p=0.001$
never opioid use	Reference group		

*Represents the ratio of means after back transformation from natural log scale
Model adjusted for age, gender, body mass index, HIV viral load, years from first HIV-positive test, alcohol consumption, use of NSAIDs and diarrhea

CONCLUSIONS

Opioid use in HIV-positive participants is associated with an increase in monocyte activation and higher inflammatory response. The underlying mechanism for this association is not known. However, it is possible that opioid use may lead to intestinal permeability and chronic systemic inflammation.