Effect of Erectile Dysfunction Drugs on T Cells and Immune Markers in Men

0877

Jee Won Park[1] , Adrian Dobs[2] , Ken Ho[3] , Frank J. Palella[4] , Eric C. Seaberg[5] , Onyebuchi A. Arah[1] , Otoniel Martínez-Maza[1] , Roger Detels[1]

[1]University of California Los Angeles, Los Angeles, CA, USA, [2]Johns Hopkins University School of Medicine, Baltimore, MD, USA, [3]University of Pittsburgh, Pittsburgh, PA, USA, [4]Northwestern University, Chicago, IL, USA, [5]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

BACKGROUND

- Erectile dysfunction (ED) drugs are frequently used in men who have sex with men (MSM)
- Although commonly associated with increased vasodilation, there is evidence of beneficial immunomodulatory effects of ED drugs in animal studies
- However, studies on the effect of ED drugs on immune capacity and function in MSM are limited
- Aim – examine the effect of ED drugs on immune cells (CD4 and CD8 T cells) and markers of inflammation in MSM over time

METHODS

Study participants:

- Multicenter AIDS Cohort Study (MACS) - ongoing prospective HIV/AIDS cohort study in the U.S. – participants from 1998 onwards
- ARRA-1 sub-study of MACS for immune markers
- Total of 1,391 HIV positive and 307 negative men (age: 19-70 years)

Measures:

- Exposure – ED drug use
- Covariates – demographic variables, pre-existing conditions, HCV infection, substance use, sexual activities, HAART, viral load
- Outcome – CD4, CD8 cell count, pro-inflammatory (IL-6, TNF-α; log-transformed), and anti-inflammatory cytokines (IL-2, IL-10; log-transformed)

Statistical Analyses:

- G-computation - to estimate causal effect of ED drugs on the outcome of interest
- Regress outcome Y at time t → $E(Y_t|A_t, L_t, Y_{t-1})$ and time-varying confounders at time t, L_t's → $P(L_t|A_{t-1}, L_{t-1})$, where A is the exposure (ED drug use)
- Using parameters from above regression, simulate to re-create *newA, newL, newY* (Y_a) → $E(Y_a|newA, newL)$
- Estimate causal mean difference (MD)

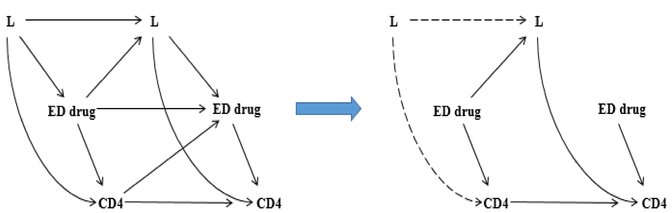


Figure 1. Directed acyclic graphs (DAGS) illustrating the pathways before and after simulation for two time points

ED drug use over time:

1) *Higher* levels of **CD4** cell counts in HIV positive men
2) *Higher* levels of **anti-inflammatory** markers
3) *Lower* levels of **pro-inflammatory** markers

RESULTS

- Adjusted causal MD of CD4 cell counts in HIV positive men after 1 year of ED drug use was 57.6 cells/μL and increased to 117.7 cells/μL after 10 years
- CD8 cell counts were higher among ED drug users over a 10-year period compared to non-users in the HIV positive group but showed almost no statistically significant differences in HIV negative group.
- HIV positive ED drug users also showed reduced levels of pro-inflammatory markers, IL-6 (MD: -1.98, 95% CI = -2.22, -1.75) and TNF-α (MD: -2.31, 95% CI: -2.48, -2.14) after one year of observation
- IL-10, was higher in ED drug users compared to non-users
- HIV negative subjects showed similar effects with ED drug use over time with respect to inflammatory markers

IMPLICATIONS

1) Residual inflammation:
- Remains a problem even after successful treatment with HAART → ED drugs may enhance immune capacity (CD4) and immunity (IL-2, IL-10)
- May also be applicable to dampen immune response (IL-6, TNF-α)

2) Promotion of healthy behaviors in MSM ED drug users:
- ED drug use with other substance use and sexual activities → May increase HIV transmission
- Nitrates/nitrites and protease inhibitors used concurrently with ED drugs → Warnings and awareness

CONCLUSION

- ED drug use was associated with a significantly higher CD4 T cell outcome in HIV positive MSM. Furthermore, analyses of immune biomarkers showed ED drug use to have been associated with lower pro-inflammatory and higher anti-inflammatory markers over time
- This observation suggests a favorable immunomodulatory effect of ED drugs in MSMs

Contact Information:
Jee Won Park, Ph.D.
kpar9173@ucla.edu

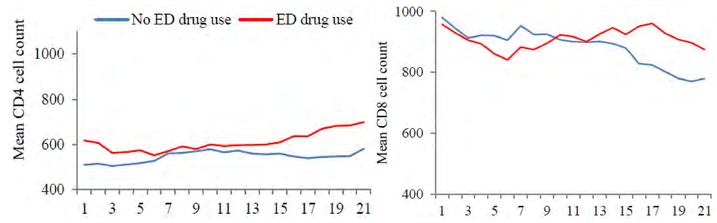


Figure 2. Mean CD4 (left) and CD8 (right) cell counts over time comparing ED drug users and non-users in HIV positive men (x-axis: MACS semiannual study visit)

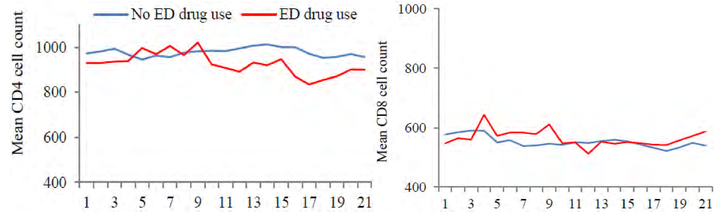


Figure 3. Mean CD4 (left) and CD8 (right) cell counts over time comparing ED drug users and non-users in HIV negative men (x-axis: MACS semiannual study visit)

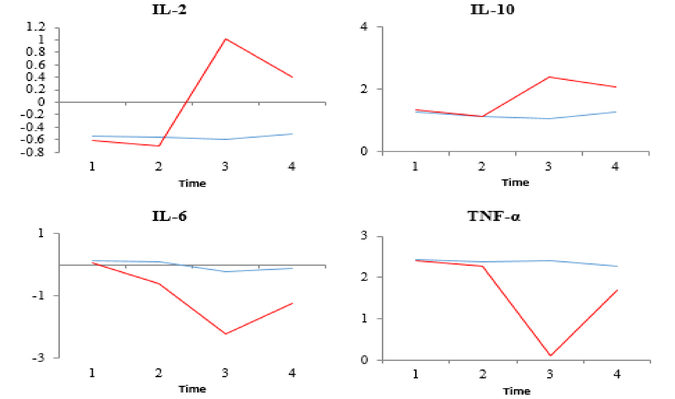


Figure 4. Mean levels of immune markers over time comparing ED drug users (red) and non users (blue) in HIV positive men

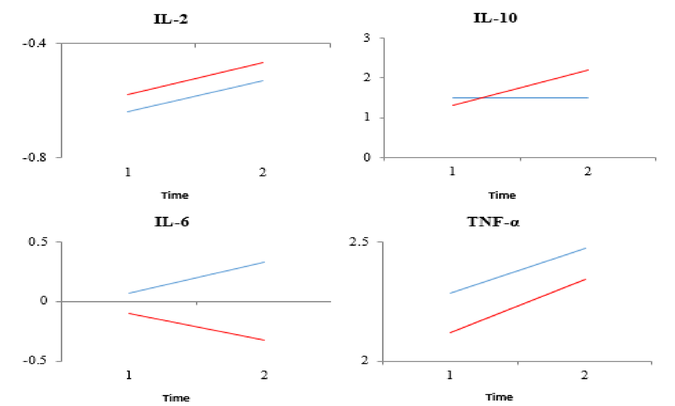


Figure 5. Mean levels of immune markers over time comparing ED drug users (red) and non users (blue) in HIV negative men